VOL. VIII. No. 3 JULY, 1946

BRITISH HEART JOURNAL

EDITORS
MAURICE CAMPBELL
EVAN BEDFORD
APPOINTED BY
THE CARDIAC SOCIETY OF GREAT BRITAIN AND IRELAND

CONTENTS

PAGE

Paroxysmal Tachycardia in Infancy and Childhood. By C. NEUBAUER 107

Traumatic Rupture of the Interventricular Septum. By TERENCE EAST 116

Multiple Chest Lead Cardiograms and their Clinical Value. By E. H. ROCHE 119

Heart Block in a Diabetic with only Mild Arteriosclerosis. By F. DARVALL 128

Arterial Thickening in Old Age. By TREVOR H. HOWELL 135

Malignant Hypertension Cured by Unilateral Nephrectomy. By C. BRUCE PERRY 139

Cardiac Output in a Case of Pericardial Effusion. By C. M. FLETCHER 143

Tuberculous Pericarditis with Effusion. By PHILIP ELLMAN 147

LONDON
BRITISH MEDICAL ASSOCIATION
TAVISTOCK SQUARE, W.C.1

PUBLISHED QUARTERLY SUBSCRIPTION 25/- PER ANNUM. U.S.A. $6.00

EDITORIAL BOARD

APPOINTED BY
THE CARDIAC SOCIETY OF GREAT BRITAIN AND IRELAND

CRIGHTON E. BRADWELL, MANCHESTER
BOYD CAMPBELL, BELFAST
JOHN COWAN, GLASGOW
SIR FRANCIS FRASER, LONDON
A. G. GIBSON, OXFORD
JOHN HAY, LIVERPOOL
HENRY MOORE, DUBLIN
JOHN PARKINSON, LONDON
K. D. WILKINSON, BIRMINGHAM
EDITOR OF *British Medical Journal*

NOTICE TO CONTRIBUTORS

Contributors who do not know the Editor's present address should send papers to

Maurice Campbell,
B.M.A. House,
Tavistock Square,
London, W.C.1.

Papers dealing with problems of the heart or of the circulation are accepted on the understanding that they have not been and will not be published in whole or in part in any other journal.

Papers sent for publication must be typed as concisely as possible with double line-spacing and a good margin. They must be accompanied by a short summary. Manuscripts should be carefully revised as alterations in print are costly and apart from slight corrections will be charged to the contributor. The author whose name comes first will receive one proof in page.

Illustrations must be ready for reproduction, except that on figures lettering which is written in pencil will be replaced by printer's type without charge. The lettering on electrocardiograms should be done in ink and they should be mounted ready for reproduction.

Where there are many electrocardiograms, only a few complexes should be shown, so that several can be mounted together, and their total width should not exceed 4½ inches, or at the most 5 inches, unless they can be reduced in size.

References to papers in the text should be made by the name of the author and the year, with or without brackets. At the end of the paper they should be arranged alphabetically, as below, according to the Harvard system:

Author's name, Initials, Year, Journal (abbreviated according to the World List of Scientific Periodicals), Volume number, Page number, e.g.:

Cowan, J. (1939). *Quart. J. Med.*, 22, 237.

Fifty reprints will be given to the author or divided among the authors on giving notice when the proof is returned. Further reprints, if desired, may be obtained from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

The subscription, 25/- per annum (20/- to members of the B.M.A.), is payable to the British Medical Association.

Applications for advertisement space should be made to the Advertisement Manager, B.M.A. House, Tavistock Square, London, W.C.1.

PAROXYSMAL TACHYCARDIA IN INFANCY AND CHILDHOOD

BY

C. NEUBAUER

From the City Hospital for Infectious Diseases, Walkergate, Newcastle-upon-Tyne

Received March 21, 1945

Occasionally in pædiatric wards and more often in private practice, one learns of cases of sudden death in infants and children. The clinical signs have not been characteristic for a diagnosis, and the autopsy has failed to determine the cause of death. Among these there are a number whose sudden death is due to paroxysmal tachycardia. Its occurrence has been considered rare in infancy and childhood, but is more frequent among children than is commonly thought. Of recent years, the number of case reports has been increasing, due to the greater interest taken in the cardiovascular diseases in childhood.

Apart from reports of isolated cases, there are only three papers dealing with more than one case. Koplik (1917) reported three cases: the first was a baby of 22 months, who had tonsillitis and bronchitis two weeks before the onset of paroxysmal tachycardia; the second was a child three years of age, and the third a child ten years old; in the last case the paroxysmal tachycardia started after a tonsillar sepsis and the attacks were observed for two years. Shookhoff *et al.* (1932) reported four cases: the paroxysms occurred in a child of eight with septic teeth; in a child of three after pertussis; in a child aged ten with an abscess of the right lower premolar and pharyngitis; and in another case three years of age. Campbell (1937) added three cases in the *Guy's Hospital Reports*: the first was a baby one month old with a temperature 101° F., but with no other definite pathological findings; the second a baby of 20 months with vomiting and liver enlargement; and in the third paroxysmal tachycardia manifested itself in a child of three years with bronchitis of two weeks standing and with otitis media. Hubbard (1941) called attention to the fact that paroxysmal tachycardia shows itself as a distinctive clinical entity in young infants, responding satisfactorily to proper treatment; he reported nine cases in infants less than one year of age.

Considering the paucity of reports on this subject it seems justifiable to give an account of the cases observed in this hospital from 1941 to 1945. It comprises eleven cases; a short clinical report, cardiographic findings, pathological, anatomical, and histological reports are given below.

Clinical signs. The onset of paroxysmal tachycardia is sudden. The attack lasts for minutes, hours, or days. The child appears acutely ill on physical examination. It is restless at the outset, but apathetic once the attack is developed, and looks pale and often cyanosed. There is respiratory distress with rapid and shallow respirations. During the attack, most commonly the heart rate is 160–200 a minute, but rates of 270 and 300 have been observed (Campbell, Langley, Lewis, Werley). Between and following attacks premature beats are often found. Signs of congestive heart failure, e.g. râles in the lungs, engorged jugular veins, and liver enlargement may develop. The pulse is often imperceptible. The temperature is usually raised. The X-ray shows pulmonary congestion and an enlarged heart in some instances.

A heart rate exceeding 190–200 in a small infant should always rouse suspicion. Too little attention is paid to a rapid heart action in babies, and that is the reason for paroxysmal tachycardia being sometimes overlooked.

Case Reports

Case 1. Three years old, admitted 13/12/1941. No previous diseases. Clinical diagnosis: nasopharyngeal diphtheria of gravis type. 60,000 units antitoxin given intraperitoneally. Heart on admission: cardiac dullness enlarged, embryocardia. The next day there was restlessness and cyanosis, and the paroxysm started (Fig. 1). The patient died the same day.

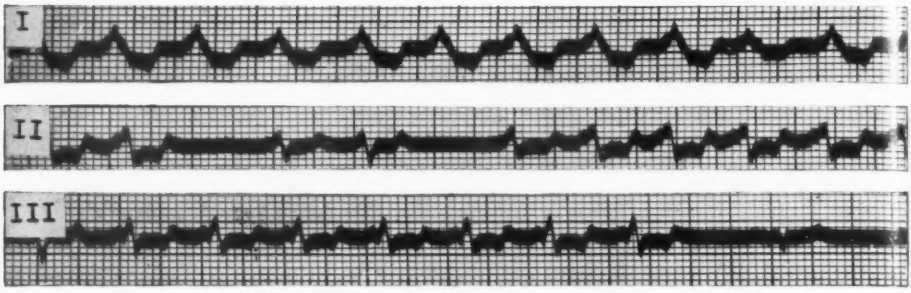


Fig. 1.—Case 1. 14/12/41. Ventricular rate 155 a minute; duration of QRS, 0·07 sec.; P–R, 0·05 sec. in lead III. This supraventricular tachycardia is considered to be of upper nodal origin.

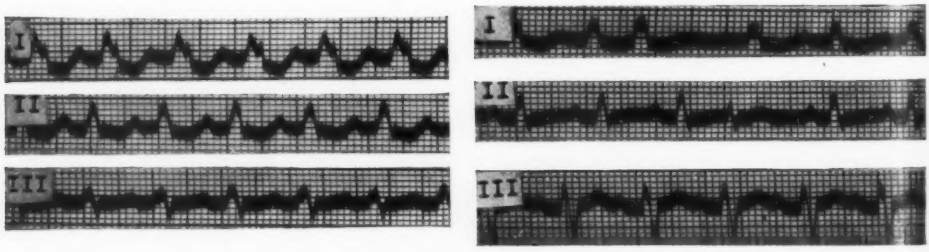
Case 2. Four years old. Admitted 27/12/1941. Previous diseases: pertussis, chickenpox, mastoid operation. Diphtheria two weeks ago. Clinical diagnosis: diphtheritic myocarditis. Heart on admission: enlarged cardiac dullness, systolic apical murmur. Second apical sound accentuated, pulse 108 a minute.

29/12/41. Onset of heart paroxysm (Fig. 2A), cyanosis, liver enlargement, albuminuria.

31/12/41. Heart action irregular due to premature beats.

1/1/42. Pulse 138. Extrasystoles. B.P. 76–48 (see Fig. 2B).

8/1/42. Heart action regular. Colour fair. Liver not enlarged, albuminuria subsiding. No murmur audible.



A B

Fig. 2.—Case 2. (A) 29/12/41. Heart action regular, ventricular rate 150 a minute, duration of QRS 0·08 sec. Supraventricular paroxysmal tachycardia. (B) 2/1/42. Sinus rhythm, ventricular rate 130 a minute; P–R, 0·17 sec. Premature beats. T flat in leads I and II. Ventricular deflections notched, voltage less than 1·5 mV. in all three leads.

Case 3. Six years old. Admitted 4/5/1942. No previous diseases. Clinical diagnosis: nasopharyngeal diphtheria of gravis type. 60,000 units antitoxin intraperitoneally. Heart normal on admission.

6/5/42. Pale and apathetic, with vomiting and an imperceptible pulse (see Fig. 3A).

7/5/42. Cardiac dullness enlarged, vomiting persistent. Attack persisted but was thought to be paroxysmal ventricular tachycardia (see Fig. 3B). The patient died two days later.

Case 4. Five years old. Admitted 14/4/1943. Previous diseases: measles. Clinical diagnosis: hæmorrhagic nasopharyngeal diphtheria of gravis type. 60,000 units antitoxin given intravenously. Blood transfusion. Heart normal on admission. B.P. 80/53.

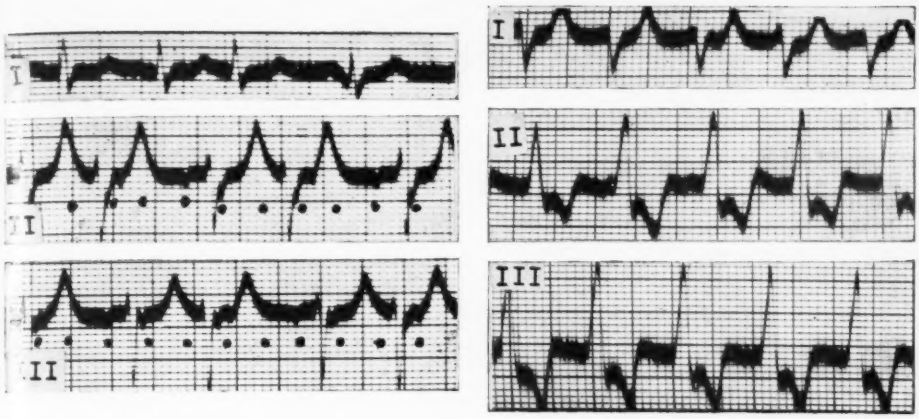


FIG. 3.—Case 3. (A) 6/5/42. Action irregular. Alternately every second and third P wave hidden within the T wave. Auricular tachycardia with 3:1 and 2:1 A-V block; A, 300; V, 130. In this and in other figures dots designate P waves. (B) 7/5/42. Action regular. Ventricular rate 140 a minute. Duration of QRS 0·10 sec. Atypical configuration of the ventricular deflection. Ventricular paroxysmal tachycardia.

18/4/42. Pale; cardiac dullness enlarged. Pulse 100. B.P. 66/42.

21/4/42. Apathetic, vomiting. Pulse 100–90 a minute.

24/4/42. Cyanosis, restlessness. Heart rate 88. Premature beats.

24/4/42. Onset of heart paroxysm, pulse imperceptible. B.P. ?38/20 (see Fig. 4). The patient died two days later.

Case 5. Four years old. Admitted 11/4/1944. Previous diseases: chickenpox. Clinical

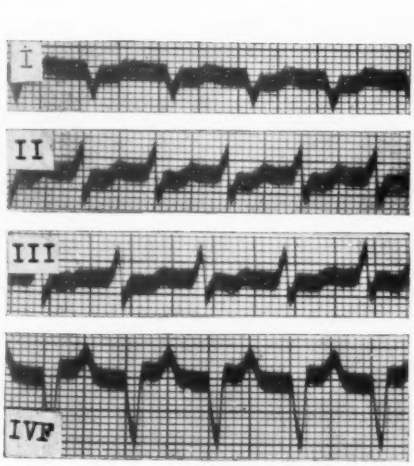


FIG. 4.—Case 4. 24/4/42. Heart action regular. Ventricular rate 160 a minute. Duration of QRS 0·08 sec. Since no P waves are visible, this supraventricular tachycardia is considered to be of nodal origin.

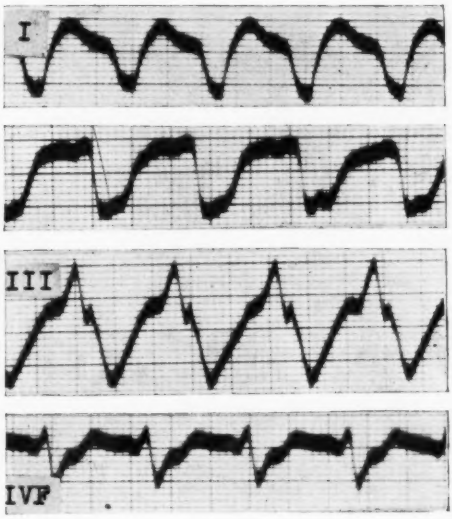


FIG. 5.—Case 5. 15/5/44. Heart action regular. Ventricular rate 120. Ventricular complexes bizarre; duration 0·23 sec. Ventricular paroxysmal tachycardia.

diagnosis: nasopharyngeal diphtheria of gravis type. 80,000 units antitoxin given intravenously. Heart normal on admission.

15/5/44. Onset of heart paroxysm (Fig. 5). Vomiting; pulse imperceptible; respiratory rate 20; albuminuria. Died.

Case 6. Five years old. Admitted 5/5/1944. Previous diseases: ?diphtheria, measles, otorrhœa. Clinical diagnosis: nasopharyngeal diphtheria of intermedius type. 40,000 units antitoxin given intramuscularly. Pulse rate 130–140. First and second sounds equal; B.P. 110/80.

11/5/44. Second apical sound greater than first. Pulse 100–108. Albuminuria.

12/5/44. Pallor, vomiting, temperature normal. Onset of heart paroxysm (Fig. 6). Died.

Case 7. Six months old. Admitted 20/6/1944. Previous diseases: bronchitis, eczema, measles a week ago. Clinical diagnosis; pertussis. Heart normal on admission. W.B.C., 56,000; 68 per cent lymphotcytes.

19/7/1944. Syncope, cyanosis. Pulse imperceptible (Fig. 7). No clinical signs of pneumonia (Fig. 7).

20/7/1944. Extreme tachycardia and tachypnœa. Temperature raised. Signs of heart failure, râles in the lungs. Died.

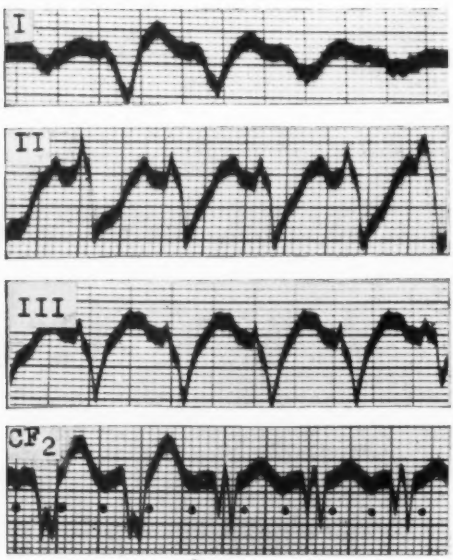


FIG. 6.—Case 6. 12/5/44. Action regular in lead II and III. Ventricular rate 143. Duration of QRS 0·12 sec. Auricular waves thought to be visible in chest lead CF_2, auricular rate 272, every second P wave hidden in the following T wave. Auricular paroxysmal tachycardia with 2:1 A-V block.

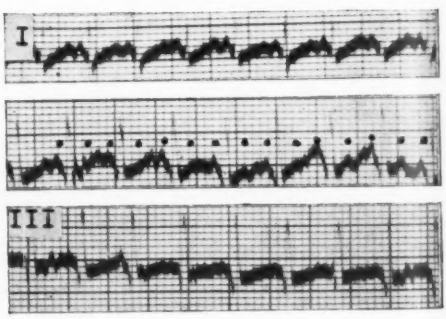


FIG. 7.—Case 7. 19/7/44. Heart action regular. Auricular paroxysmal tachycardia with possible 2:1 conduction : A, 460; V, 230.

Post-mortem report. (From the Department of Pathology, University of Durham.)

Pericardium, smooth and glistening. Heart, 52·0 g. (Mean weight at this age 31·0 g.) Epicardium quite smooth. Right auricle dilated and filled with agonal clot; no thrombus in appendix. Foramen ovale completely closed. Tricuspid leaflets thin and delicate. Right ventricle slightly dilated; wall 0·3 cm. thick. Pulmonary valves thin and delicate. Pulmonary artery smooth and elastic. Left auricle empty; no evident dilatation; no thrombus in appendix or elsewhere. Mitral leaflets thin and delicate. On anterior leaflet 0·2 cm. from the free margin there is an " angioma "; about 0·2 cm. from it is another one which appears to have

healed. Left ventricle not dilated; very little clot; wall 0·7 cm. thick. Aortic leaflets thin and delicate. Orifices of coronary arteries patent. Ductus arteriosus closed. Aorta smooth and elastic. Myocardium firm but greyish and pink.

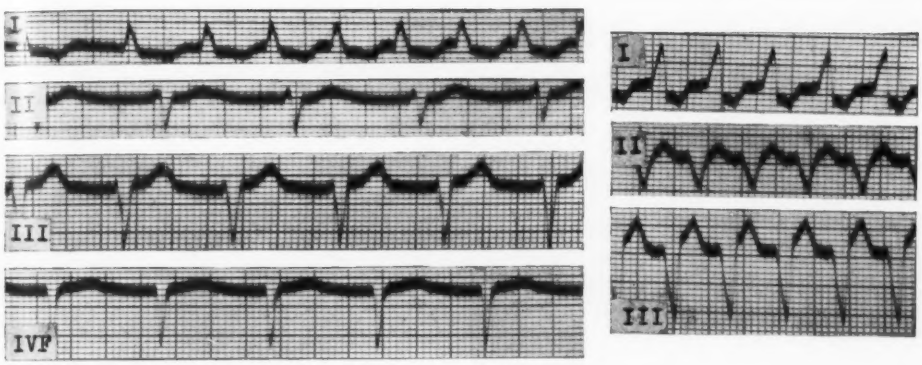
Histology. A topographical survey of the heart, including epicardium, right and left auricles, mitral and tricuspid valves, annulus fibrosus, auriculo-ventricular sulcus, right and left ventricles, was made and there was no trace of any form of myocarditis. Special staining showed a mild grade of diffuse fatty degeneration of the myocardium which could be due to many forms of toxæmia.

Case 8. Three years old. Admitted 18/10/1944. Previous diseases: rubella, pertussis. Clinical diagnosis; hæmorrhagic nasopharyngeal diphtheria and *S. hæmolyticus* infection. 50,000 units antitoxin intravenously. Blood transfusion. Heart normal on admission.

21/10/44. Runs of premature beats and short paroxysm (Fig. 8A). B.P. 85/38. Albuminuria.

24/10/44. Onset of longer paroxysm. Pulse too fast to count (Fig. 8B).

26/10/44. Extremities icy-cold. Liver enlargement. B.P. could not be measured. Patient died.



A B

FIG. 8.—Case 8. (A) 21/10/44. Onset of supraventricular paroxysmal tachycardia in lead I. Ventricular rate 171. The paroxysm has subsided in lead II, the rate being 82. There are no P waves visible, the heart action is regular especially in lead III, in which the ventricular rate is 100. Duration of QRS 0·10 sec. The paroxysm in lead I and the rhythm in lead II and III are considered to be of nodal origin. (B) 24/10/44. Heart action regular. Ventricular rate 188, duration of QRS 0·11 sec. Left ventricular preponderance. Ventricular paroxysmal tachycardia.

Post-mortem report. (From the Department of Pathology, University of Durham.)

Heart. Weight 90 g. (fixed in formalin). Right auricle slightly dilated, containing a large amount of post-mortem thrombus. Auricular appendage contains adherent mural thrombus. Foramen ovale closed. Tricuspid valve admits two fingers: cusps thin and delicate. Right ventricle slightly dilated and contains post-mortem thrombus. Endocardium shows hæmoglobin staining; muscle, 0·3 cm. thick at the base. Pulmonary valve shows marked hæmoglobin staining of its cusps. Coronary artery normal apart from hæmoglobin staining. Left auricle healthy: no mural thrombi. Mitral valve admits one finger and cusps thin and delicate. Left ventricle dilated with some endothelial hæmorrhages on the interventricular septum: muscle at the base 0·7 cm. thick. Aortic valve healthy. Coronary arteries patent. Myocardium, no obvious fatty change.

Histology. Heart: left auricle, mitral valve, left ventricle. Intense veno-capillary congestion in the myocardm together with a sparsely but widely distributed fatty degeneration. No evidence of myocarditis or valvulitis.

Right auricle, tricuspid valve, right ventricle. Recent mural ante-mortem thrombus in appendix, but apart from this changes similar to those in the left side.

Auriculo-ventricular node; similar changes but no inflammation.

The appearance here pointed to an acute and intense cardiac failure, the cause of which is not apparent from this material.

Case 9. Four years old. Admitted 1/12/44. No previous diseases. Clinical diagnosis: meningo-encephalitis. Heart normal on admission, no consolidation in the lung. W.B.C., 16,800; 74 per cent polymorphs and 21 per cent lymphocytes.

7/12/44. Pulse 124. B.P. 105/65. Lung: no apparent disease.

9/12/44. Onset of heart paroxysm, pulse too fast to count (Fig. 9). Temperature 100° F., signs of consolidation in the lung. Died.

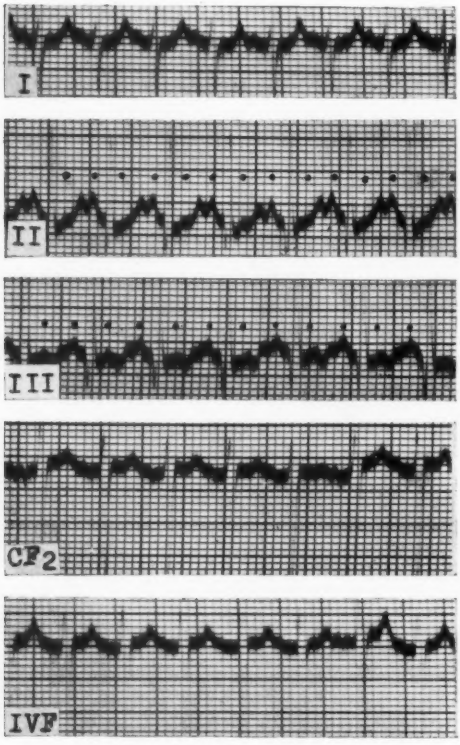


FIG. 9.—Case 9. 9/12/44. Heart action regular. Auricular rate 376, ventricular rate 188. Alternate P waves hidden within the S–T transition. Paroxysmal auricular tachycardia with 2:1 A-V block.

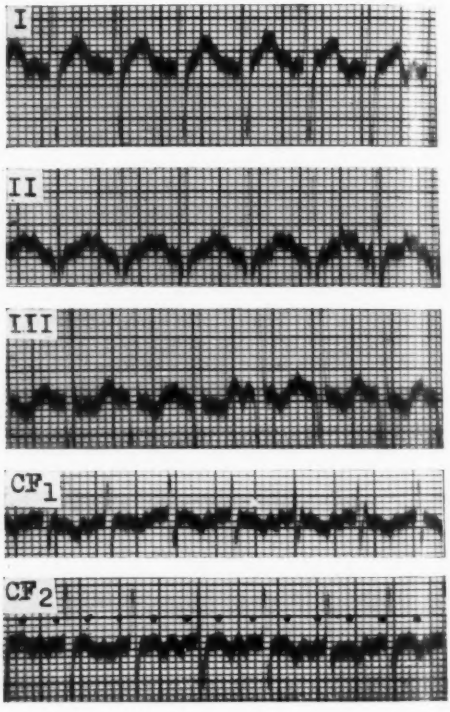


FIG. 10.—Case 10. 18/2/45. Action regular. Ventricular rate 176. Auricular rate 352. Both auricular waves are hidden within the S–T–T complex. Paroxysmal auricular tachycardia or flutter with 2:1 A-V block.

Post-mortem report. (From the Department of Pathology, University of Durham.)

Anatomical diagnosis: Acute suppurative meningitis. Acute bronchopneumonia. Accidental involution (thymus).

Pericardial sac, smooth and glistening.

Thoracic aorta, quite smooth and elastic.

Heart. Weight 75 g. (fixed in formalin). Pericardium smooth and glistening: no gross abnormality. Right auricle empty. Foramen ovale completely closed. Tricuspid leaflets thin and delicate. Right ventricle a small amount of post-mortem clot: wall 0·3 cm. thick. Pulmonary valves thin and delicate. Pulmonary artery smooth and elastic. Left auricle empty. Mitral leaflets thin and delicate. Left auricle empty, but dilated: wall 0·9 cm. thick. Pulmonary leaflets thin and delicate. Orifices of coronary arteries patent. Myocardium distinctly pale and turbid in appearance.

Histology. Heart (left auricle, myocardium, left ventricle): no evident abnormality.

Case 10. Four months old. Admitted 13/2/45. Previous diseases: otorrhœa. Clinical diagnosis: epidemic cerebrospinal meningitis. Heart on admission: tachycardia. Pulse volume poor.

17/2/45. Slight vomiting. B.P. 98/40. W.B.C.: 24,000; 61 per cent polymorphs and 25 per cent lymphocytes.

18/2/45. Onset of heart paroxysm (Fig. 10).

20/2/45. Heart action regular, rate 150 a minute.

22/2/45. Cardiac dullness enlarged, pulse volume good.

1/3/35. Heart: no apparent disease.

Case 11. Five months old. Admitted 15/2/45. No previous diseases. Has been ill for the last five days, but no clinical signs could be found. The baby's mother had a sore throat a few weeks ago, and a child in the same family got scarlet fever two weeks ago; because of this the baby was given scarlet antitoxin and sulphonamide before admission. Heart on admission: action too fast to count. Lung: no apparent disease. Clinical examination did not reveal any signs of a *S. hæmolyticus* infection.

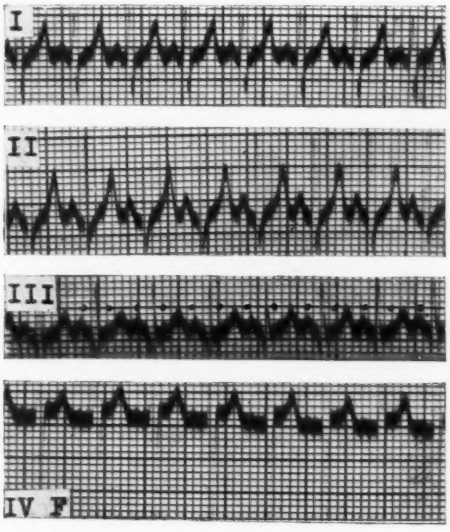


FIG. 11.—Case 11. 15/2/45. Heart action regular. Ventricular rate 222, auricular rate 444. Paroxysmal auricular tachycardia with 2:1 A-V block.

16/2/45. Colour grey, eyes sunken, hands cold. Lung: no consolidation: X-ray negative. Bacteriological findings negative. Patient died.

DISCUSSION

Eleven cases of paroxysmal tachycardia are reported in the present series. The age of the patients was under one year in 3 cases, and from three to six years in 8 cases.

The heart condition was associated with various infections: a diphtheritic infection of gravis or intermedius type was present in seven cases, pertussis was found in another, meningitis in two more, but no infectious focus could be traced in the last case, a baby five months old. These findings leave little doubt that paroxysmal tachycardia in childhood occurs more often in the presence of an infection than in its absence. Koplik assumed that the first attack of influenza in one of his cases was the starting point of the paroxysm, and that the cardiac collapse of the first paroxysm was the forerunner of the subsequent paroxysms. The infective origin is obvious in Shookhoff's cases, e.g. in one child while convalescing from pertussis. Hauser (1921) referred to pertussis as a cause of paroxysmal tachycardia. Hubbard admits

that paroxysmal tachycardia may be associated with some other illness, but he believes it may start with no other evident cause. One child in Campbell's series probably had a diphtheria prior to the onset of the paroxysmal tachycardia.

The attack sets in suddenly. There are runs of premature beats lasting for a few seconds, heralding the onset of the paroxysm in some instances (see Fig. 8A). Frequent premature beats may also occur when the attack terminates (see Fig. 2B).

The main clinical signs enumerated in order of their frequency in the present series are the following: imperceptible pulse (6 cases), lowered systolic and diastolic blood pressure (5), vomiting (4), cyanosis (4), albuminuria (4), enlarged cardiac dullness (4), pallor (3), liver enlargment (2), apathy (2), raised temperature (2), syncope (1), embryocardia (1), systolic apical murmur (1), râles in the lung (1), and restlessness (1).

There are two cases in the present series which are of the type described by Hubbard (Cases 7 and 11), occurring in babies of six months and of five months. Pallor, restlessness, raised temperature, and the paroxysm being the signs of the onset, followed by signs of a failing heart the next day. No consolidation in the lung is found on clinical or X-ray examination. Attacks similar to those described might be mistaken for pneumonia; tachypnœa, cyanosis, and a raised temperature readily suggest a diagnosis of pneumonia.

Cardiographic findings. Auricular paroxysmal tachycardia and auricular flutter are closely related. Campbell found paroxysmal flutter to be more frequent in infants than in adults, and he regarded it as more common in infants than all varieties of simple paroxysmal tachycardia combined. Koplik's Case 3 was an example of auricular flutter. Three out of four cases of paroxysmal tachycardia reported by Shookhoff were auricular flutter. He gives a review of 40 cases of paroxysmal tachycardia occurring in children and published by different authors up to 1932. These cases presented themselves as ventricular paroxysmal tachycardia, 1 instance; auricular paroxysmal tachycardia, 5 instances; nodal paroxysmal tachycardia, 2 instances; paroxysmal auricular flutter, 12 instances; undiagnosed paroxysmal tachycardia with a rate of 200 or more, 18 instances.

Campbell regarded his Case 3 as probably flutter with 1:1 response. Up to-day it has been held that paroxysmal tachycardia is found with an auricular rate varying between 160 to 240, while auricular flutter is associated with higher auricular rates of about 300 a minute. Furthermore it was thought that auriculo-ventricular block is characteristic of auricular flutter, but was considered uncommon in paroxysmal tachycardia. This no longer holds good as A-V block is found in auricular tachycardia as well (Barker *et al.*, 1943; Decherd *et al.*, 1943; and Evans, 1944). It was found in two instances (Cases 3 and 6) in the present series. Chest leads proved to be more reliable in demonstrating auricular activity than the limb leads. In our experience chest leads are more useful in the examination of adults than of babies and infants. The comparatively small size of the heart and chest wall in this early age of life seems to be the reason for the difficulty in applying an electrode to a selected area of the heart. Fig. 6 shows that a chest lead might reveal auricular activity while there are no certain signs of auricular activity in the limb leads. In most cases, however, the limb leads in babies and infants show the auricular waves as well or in some instances even better than the chest leads. Lewis (1912) and Carr (1932) found that paroxysmal tachycardia may change into auricular flutter, which suggests some relationship.

Ventricular paroxysmal tachycardia. There were three records in the present series. The duration of QRS is prolonged, and QRS is not accompanied by P waves. The configuration of the ventricular deflections is such that it may be difficult to distinguish the QRS from the S–T–T.

Nodal paroxysmal tachycardia. Three records were found in the present series. The ventricular rate varies between 150 to 160 a minute.

Sinus tachycardia is readily distinguished from paroxysmal tachycardia by the presence of P waves and a normal P–R interval which may normally be of 0·08 sec. duration in babies and infants.

Pathological anatomy and histology. It is remarkable that distinctive pathological changes either in the myocardium or in the conductive tissue have not been found in three cases of the present series, where an autopsy was performed. Two were cases of paroxysmal auricular

tachycardia or flutter with 2:1 block, one of paroxysmal ventricular tachycardia. The pathological findings in these three showed no evident abnormality, no trace of myocarditis or valvulitis, though the appearances pointed to an acute and intense cardiac failure in one instance. This is of great practical importance; it is obvious that paroxysmal tachycardia has to be diagnosed during life or it will not be diagnosed at all, the post-mortem examination showing no pathological changes.

The prognosis is grave in infants and very grave in cases in which the underlying infection is severe, e.g. in diphtheria of gravis type. In milder cases, the attack may stop spontaneously.

Treatment. Digitalis given promptly may have an effect in some instances, and save the child's life. Koplik had this impression in one of his cases. Hubbard reports very good results. The treatment with digitalis had no chance in the diphtheria cases of the present series. In only one (Case 2) was the result satisfactory. In a case of meningitis (Case 10), flutter was changed into fibrillation and this came under control by digitalis treatment. The results with other drugs recommended for treatment of paroxysmal tachycardia, e.g. quinidine and magnesium sulphate intravenously are also not always satisfactory. Further, it was found that pressing on the carotid sinus or the eyeball, which may stop an attack in an adult, were not effective in infants.

This report gives a rather poor prognosis for paroxysmal tachycardia in infancy and childhood. It must not be forgotten, however, these investigations were carried out on children admitted with or suspected of severe acute infective diseases. Where a mild infection may have been the causative factor the response to treatment, and thus the prognosis is probably much better.

Summary

Paroxysmal tachycardia occurs more often in infancy and childhood than is commonly thought, and it accounts for some instances of sudden and unexplained death in infancy.

Clinical and cardiographic signs of eleven cases and pathological anatomical and histological findings of three autopsies are reported.

Prognosis and treatment are discussed.

It is with kind permission of Professor A. F. Bernard Shaw, Department of Pathology, University of Durham, that the post-mortem notes are included with the present report.

I wish to thank Dr. McCracken, M.O.H., Newcastle-upon-Tyne and Dr. E. F. Dawson-Walker, former Medical Superintendent of the City Hospital for Infectious Diseases, Walkergate, for facilities granted.

References

Barker, P. S., Wilson, F. N., and Johnston, F. D. (1943). *Amer. Heart J.*, **26,** 435.
Berry, E. H. J. (1940). *Lancet*, **238,** 29.
Campbell, M. (1937). *Guy's Hosp. Rep.*, **87,** 205.
Carr, F. B. (1932). *Amer. Heart J.*, **7,** 668.
Decherd, G. M., Herrmann, G. R., and Schwab, E. H. (1943). *Ibid.*, **26,** 446.
Evans, W. (1944). *Brit. Heart. J.*, **6,** 233.
Hauser, O. (1921). *Klin. Wschr.*, **48,** 172.
Hubbard, J. P. (1941). *Amer. Dis. Child.*, **61,** 687.
Katz, L. N. (1941). *Electrocardiography*, Philadelphia.
Koplik, H. (1917). *Amer. J. med. Sci.*, 834.
Lewis, T. (1915). *Heart J.*, **1,** 98.
Neubauer, C. (1942). *Brit. med. J.*, **2,** 91.
—— (1943). *Brit. J. Child. Dis.*, **1,** 3.
Poynton, F. J. and Wyllis, W. G. (1926). *Lancet*, **2,** 371.
Russel, H. B. and Ellison, J. B. (1927). *Ibid.*, **2,** 546.
Shookhoff, C., Litvak, A. M., and Matusoff, T. (1932). *Amer. J. Dis. Child.*, **43,** 93.
Gibson, St. (1943). *In Brennemann*, Pædiatrics.
Willis, F. A. and Amberg, E. (1929). *Amer. J. Dis. Child.*, **38,** 557.

TRAUMATIC RUPTURE OF THE INTERVENTRICULAR SEPTUM

BY

TERENCE EAST

Received April 12, 1945

The results of damage to the heart from indirect violence have aroused a good deal of interest in recent years, for in many cases modern methods of investigation have increased the possibilities of diagnosis. The account of this unusual case seems worthy of record.

A young man of nineteen years had a head-on collision with a lorry when driving a motor car. He was thrown forcibly against the steering wheel and hurt the front of his chest. Breathing was rather painful, but no bones were broken. He was in hospital for a fortnight. No cardiac murmur was noted. On returning home later he was examined by his family doctor and a murmur was heard. He was then referred for further examination. Three months before the accident he had been passed by a medical board for the R.A.F.

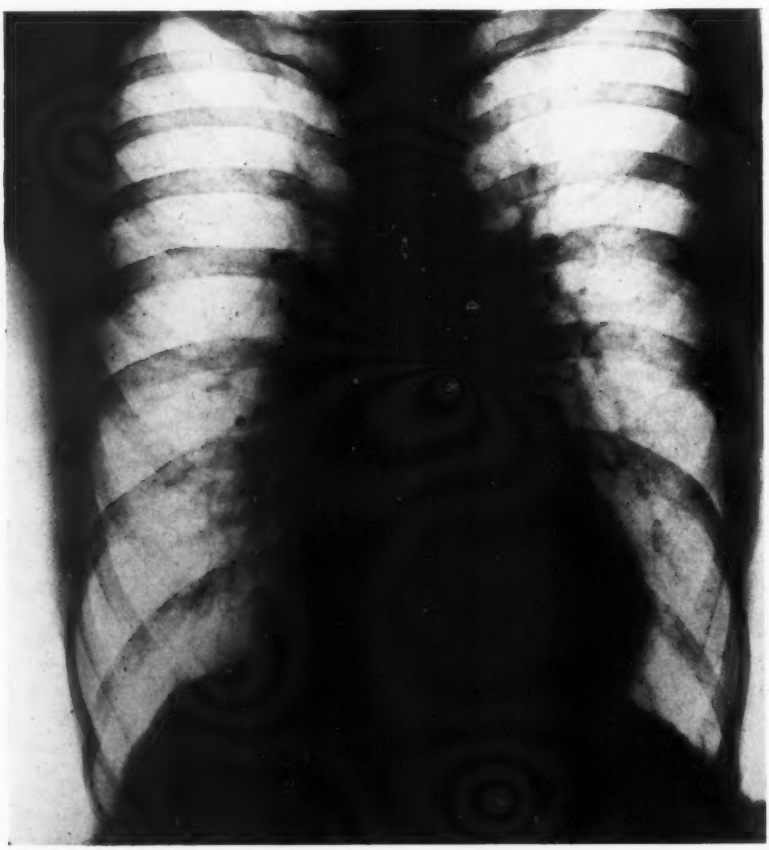


FIG. 1.—Teleradiogram of the heart, showing no abnormality except a little enlargement to the right.

The patient was a tall thin youth with rather a flat chest, somewhat depressed just to the left of the sternum. The apex beat was in the fifth left space, four and a half inches to the left of the mid-line. It was rather increased in force and rate from nervousness. An intense rough systolic murmur was audible all over the præcordium, loudest about the left edge of the sternum in the fourth left intercostal space. It was not conducted in any particular direction. A strong systolic thrill accompanied the murmur. The mitral first sound was faintly reduplicated until the rate slowed down; a faint third sound followed the mitral second, but only on acceleration. The pulmonary second sound was rather loud. The

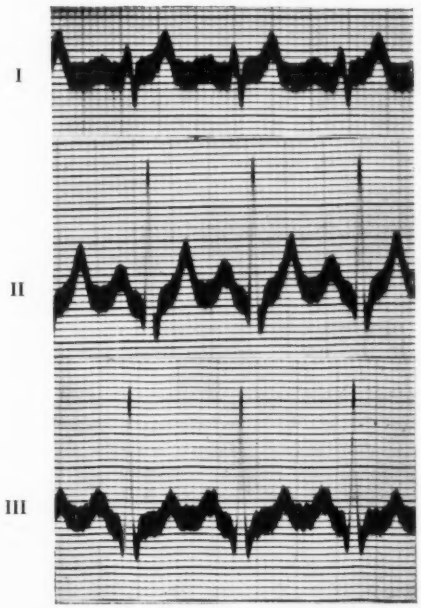


FIG. 2.—Electrocardiogram, showing some right axis deviation.

blood pressure was 140/90. There was no dullness to the right of the sternum. There was no cyanosis, nor engorgement of the jugular veins or liver. He had no symptoms. At the time it was not possible to take a cardiogram or a skiagram.

Three and a half years later he was seen again. He had had no symptoms and was following a quiet occupation in a technical laboratory. The physical signs had not changed at all. The blood pressure was 120/80. Screening showed that the left auricle had a normal contour, without any systolic pulsation during ventricular systole. The antero-posterior view is shown in the illustration; the right side seems to be a little enlarged (Fig. 1). The cardiogram shows slight right axis deviation (Fig. 2).

Discussion

It is certain that the murmur was not there before the accident. It seems to have developed as a result of the blow on the chest; not at once, but after a latent period, perhaps about a fortnight. No symptoms accompanied the appearance of whatever lesion it is due to. Such a thrill and murmur may suddenly appear in the heart from three possible causes, and they may all arise from indirect violence.

Rupture of a chorda tendinea of the mitral valve usually results from disease. Bailey and Hickham (1944) describe cases in which there was the sudden appearance of a mitral systolic murmur and thrill between the apex and the left border of the sternum, conducted to the axilla. The left auricle becomes enlarged and may pulsate. Failure may develop,

with fibrillation, soon or only after years. Frothingham and Hass (1934) have described the rupture of a normal chorda from indirect violence.

Rupture of a papillary muscle of the mitral valve is usually a very grave occurrence. The same signs are produced. In the case of Glendy and White (1936) trauma was the cause. It may occur after infarction (Morargues, 1939). In Anderson's case (1940) there were a systolic murmur and thrill conducted to the axilla; at first there was failure but later a good recovery. The site of the murmur suggests that it was due to the rupture of a valve, but one cannot entirely exclude the septum. For the most part rupture of a papillary muscle of the mitral valve is more serious than rupture of a chorda tendinea, and leads to the onset of rapid fatal failure. Perforation of the interventricular septum is met with from time to time after myocardial infarction. I have seen it arise from an abscess. There may be symptoms of pain, shock, and dyspnœa (Stanley, 1937), with the rapid appearance of failure of the right ventricle. On the other hand there may be no symptoms at all, and but little ill-effect (Wood, 1944). A mid-præcordial thrill and murmur at systole are usually described, such as are produced by the congenital lesion. The acquired perforation is usually low down in the septum (Gross and Schwartz, 1936). Damage to the myocardium may cause angina pectoris (Campbell, 1939). The contused area may become the site of an aneurysm (O'Farrell, 1939) and perhaps rupture later. Indirect violence to the heart may damage the septum itself ; for partial heart block has been recorded from the effects of blast (Campbell, 1943), and from a crushing injury (Barber, 1942); complete block has also been noted (Coffer *et al.* 1941).

The signs in this case suggest that rupture of the interventricular septum occurred. The site of the thrill and murmur and the absence of any effect on the left auricle or on the efficiency of the heart are in favour of this diagnosis. One might suggest that the septum softened, and ruptured some time after the accident, perhaps giving way gradually, so that no sudden disturbance occurred. If the membranous portion had given way, this would probably have happened at once. In any case it is most unlikely to do so unless it is the site of a congenital aneurysm.

The original description of Henri Roger (1879) is worth recalling, for he made his diagnosis some years before an autopsy confirmed it. He described " a murmur loud and long; it is single, begins at systole, and is prolonged so as to hide the natural tic-tac; it has its maximum, neither at the apex, nor at the right base, nor at the left, but in the upper third of the præcordial region; it is median, like the septum itself; and from this central point it diminishes evenly in intensity and by degrees, accordingly as one gets further away from it; it is local and without propagation into the vessels. It coincides with no sign of organic disease other than the thrill. An abnormal murmur which comprises this combination of character is the pathognomonic sign of patency of the septum of the ventricles." The remark of one of those who heard this communication of course applies to the case described here. " C'est là une circonstance regrettable, il faudrait au moins une observation avec autopsie."

Conclusion

With this precedent of Roger, the proposed diagnosis is traumatic rupture of the interventricular septum. The history and physical signs in such a case are described.

References

Anderson, R. G. (1940). *Brit. med. J.*, **2**, 307.
Bailey, O. T., Hickham, J. B. (1944). *Amer. Heart J.*, **28**, 578.
Barber, H. (1942). *Brit. Heart J.*, **4**, 83.
Campbell, M. (1939). *Ibid.*, **1**, 177.
Campbell, M. (1943). *Ibid.*, **5**, 163.
Coffer, T. H., Rush, H. P., Miller R. F. (1941). *North West Med.*, **40**, 195.
Frothingham, C., Hass, G. M. (1934). *Amer. Heart J.*, **9**, 492.
Glendy, R. E., White, P. D. (1936). *Ibid.*, **11**, 366.
Gross, H., Schwartz, S. D. (1936). *Ibid.*, **11**, 626.
Morargues, V. (1939). *Ibid.*, **17**, 106.
O'Farrell, T. (1939). *Brit. Heart J.*, **1**, 172.
Roger, H. (1879). *Bull. Acad. Med., Paris*, **8**, 1091.
Stanley, D. F. (1937). *Amer. Heart J.*, **14**, 240.
Wood, A. M. (1944). *Brit. Heart J.*, **6**, 191.

MULTIPLE CHEST LEAD CARDIOGRAMS AND THEIR CLINICAL VALUE*

BY

E. H. ROCHE

From the Electrocardiographic Department, Auckland Public Hospital, New Zealand

Received May 2, 1945

The following is a brief contribution to the study of multiple chest lead cardiograms and an assessment of their diagnostic value in a series of 302 cases.

The cardiogram obtained by placing an electrode on the surface of the heart and pairing it with an electrode placed upon a distant part of the body was studied in experimental animals by Lewis and Rothschild in 1915. This pioneer work laid the foundation of modern chest lead cardiograms. The essential parts of Lewis and Rothschild's work were confirmed by numerous animal experiments and by a unique clinical test performed on an exposed human heart by Barker, McLeod, Alexander, and Wilson in 1929. Subsequent investigations have been made by Wolferth and Wood, 1932; Wilson, Hill, and Johnston, 1934; Johnston, Hill, and Wilson, 1935; Kossmann and Johnston, 1935; Wilson, Johnston, and Hill, 1935; Wood and Selzer, 1939; Evans, 1939; and Wilson *et al.*, 1944; these have gone far to elucidate the præcordial cardiogram in normal and abnormal hearts and to show that the tracings obtained from the præcordium are essentially the same as those obtained direct from the underlying pericardial surface.

In putting together the following notes, wherein an attempt is made to explain the initial deflections of the præcordial electrocardiogram, the experimental work of these investigators has been freely drawn upon. The form of any cardiogram depends primarily upon the fact that, although the muscle fibres in the heart follow an oblique or circuitous course, the frequent branching and inter-communication between them enables the wave of excitation to pass fairly directly from the endocardial to the pericardial surface. In fact, having quickly traversed the Purkinje system, the excitatory process appears to spread almost centrifugally outwards from the ventricular cavities. We may, therefore, visualize during the QRS interval a wave of positive potential followed closely by a wave of negative potential spreading outwards from each ventricular cavity. These positive and negative charges are held apart by an electromotive force similar to that between the poles of a battery. The contracting muscle over which the wave has passed and the quiescent muscle ahead of the wave behave as normal electrical conductors. Thus the negative potential generated at the proximal side of the wave is conducted backwards to the ventricular cavities and the positive potential generated at the distal side of the wave is conducted outwards to the pericardial surface of the ventricles, but they are not able to neutralize each other by passing in the reverse direction across the wave of excitation. On the contrary, the difference of potential appears to increase as the wave travels so that, within limits, the thicker the ventricular wall, the greater will be the potential difference between its endocardial and pericardial surfaces. Also, where the heart is nearest to the chest wall, its potential will reach an overlying præcordial electrode with the smallest amount of loss in transmission.

From the foregoing principles it follows that the ventricular cavity remains negative so long as the wave of excitation is spreading through any part of the heart muscle, i.e. throughout the QRS interval, after which it returns quickly to zero potential. It is also clear that the pericardial surface is positive for at least part, and nearly always the first part, of the QRS interval. At any point on the pericardial surface, however, the potential switches suddenly to that of the ventricular cavity as soon as that point is reached by the wave of excitation, the

* Read before a Meeting of the Royal Australasian College of Physicians at Christchurch, New Zealand, on February 16, 1945.

underlying muscle then behaving as a normal electrical conductor. The negative potential of the ventricular cavities is conducted backwards, upwards, and to the right through the auricles and great vessels and is transmitted chiefly to the right upper quadrant of the body which consequently remains negative throughout the QRS interval. Some of the negative charge is, however, conducted forwards from the right auricle and tends to neutralize the positive potential of the adjacent right ventricular pericardium. The positive potential of the pericardial surface of the ventricular muscle on the other hand is chiefly conducted forwards and downwards and to the left, and so dominates the electrical field in the front, left lower, and (usually to a lesser extent) the left upper quadrants of the body.

The initial ventricular deflections of the normal præcordial cardiogram consist of an upstroke (ascending limb of R) followed by a deep rapid downstroke (intrinsic deflection of Lewis, descending limb of R and S) and then a return to the iso-electric line. The upstroke is made by the rise of positive potential at the pericardial surface underlying the electrode as the wave of excitation approaches. The intrinsic deflection is made by the rapid switching of the potential at the pericardial surface to that of the ventricular cavity and signalizes the arrival of the wave of excitation at the point on the pericardial surface underlying the electrode, and the return to the iso-electric line is made by the disappearance of the negative potential of the ventricular cavities which may be rapid or relatively gradual according to whether the excitatory process is still spreading through other parts of the heart. Generally speaking, as the examining electrode is moved from right to left across the præcordium it draws closer to the heart muscle which at the same time becomes thicker. When it has passed the septum it begins to move further away from the bifurcation of the bundle and when it has passed the apex it begins to move further away from the surface of the heart. Hence, with a certain reservation that will be mentioned later, the R wave in the cardiogram becomes progressively higher as the electrode moves from the right border to the apex, after which it becomes lower, and it occurs progressively later as the electrode moves from the septum to the axilla.

Frequently the onset of the excitatory process in the septum and adjacent parts of the ventricular wall causes the ventricular cavity to become slightly negative before the impulse has finished spreading through the most distant parts of the Purkinje network. In this event, when a tracing is taken from the left side of the præcordium the negative potential is conducted electrically from the cavity through the as yet quiescent muscle underlying the electrode and causes a negative deflection (descending limb of the Q wave) in the cardiogram. The R wave then occurs relatively late in the QRS interval and the arrival of the wave of excitation at the pericardial surface underlying the electrode will mark the end or very nearly the end of the excitatory process in the heart. It will therefore mark the end or very nearly the end of the negative potential in the ventricular cavities. Thus the intrinsic deflection in the cardiogram will terminate at or very near the base line and there will be little or no S wave. The behaviour of the T wave is still in some cases obscure. Although it is well known that during the T wave the myocardium is relaxing, the nature of this process and its variations from normal are not so clearly understood. Its interpretation, therefore, remains to some extent empirical.

Characteristic variations from the normal QRS complexes are produced by certain forms of ventricular hypertrophy or damage. In the case of left ventricular preponderance the normal differences between the two sides of the præcordium are increased. On the right side of the præcordium the positive potential is apparently neutralized by the increased negative potential generated in the left ventricle and conducted from the cavity of that ventricle through the auricles and adjacent tissues. Consequently the R wave is very small or absent and the S wave is deeper and somewhat wider than usual. Complexes of this type extend well across the præcordium and may be obtained from the apex. Still further to the left the R wave suddenly becomes abnormally high and rather wide and tends to occur rather late, and is therefore frequently preceded by a Q wave. The transition from the small to the high R wave observed in the 3rd, 4th, or 5th chest lead is marked by inversion of the T wave.

In right ventricular preponderance the R wave is highest on the right side of the præcordium usually in the 2nd or 3rd chest lead, where T is frequently inverted and Q may be present, S is small or absent. In this condition leads from the left side show a small R similar to that normally found on the right side and S is correspondingly deep; T is upright.

In bundle branch block the septum on the affected side distal to the block remains quiescent until the excitatory process from the unaffected side has spread through the septum. While the septum is the seat of a spreading excitatory process, positive potential is generated upon its quiescent surface. This is conducted through the cavity and free wall of the ventricle and results in a small R wave on the affected side of the prækordium. The completion of the excitatory process in the septum causes the potential of the affected side to switch to that of the opposite ventricular cavity. This negative potential causes an S wave or a notch upon the R wave in tracings from the prækordium on the affected side. The subsequent spread of the excitatory process in the free wall of the affected ventricle causes a second rise of positive potential which reaches the chest wall far out on the affected side. There will thus be a secondary R wave which may be followed by a more or less normal intrinsic deflection or the return to the base line may be rather slurred. In the case of left bundle branch block the secondary R wave is frequently obtained only from the axillary leads. Tracings from the prækordium overlying the normal bundle differ from the normal cardiogram only in that the R wave is small or absent and the return of the S wave to the iso-electric line is delayed. The widening of S is due to the late excitatory process in the opposite ventricle, the negative potential generated therein being conducted across the septum and through the cavity and contracting free wall of the normal ventricle, and so to the prækordium.

In myocardial infarction the damaged muscle conducts electricity in a normal manner, but cannot respond to the wave of excitation. If the infarct involves the whole thickness of the ventricular wall, the potential of its pericardial surface must at all times be that of the ventricular cavity. It is therefore negative throughout the QRS interval and there is no R wave in the cardiogram from that region. The T wave is inverted over the infarct and over a region surrounding the infarct where the myocardial changes are of minor degree. If the infarct involves the endocardial surface, but not the whole thickness of the ventricular wall, the negative potential of the ventricular cavity is at first conducted through infarct and normal muscle to the surface of the chest, and the first part of the QRS complex consists of a Q wave. Then, as the wave of excitation, spreading outwards around the periphery of the infarct, reaches and spreads through the normal muscle between the infarct and the pericardial surface an upstroke will be registered which may or may not go above the base line. On the arrival of the excitatory process at the pericardial surface overlying the infarct there is a return to zero potential unless the excitatory process is still spreading through other parts of the heart, in which case there will be a secondary negative wave.

From these considerations it will be apparent that the QRS complexes of the prækordial cardiograms, unlike those of the standard leads whose interpretation is still largely empirical, lend themselves to rational interpretation and that most of the common findings can be explained in terms of myocardial pathology.

Results Obtained

Before proceeding to analyse a series of cardiograms, certain points of technique call for consideration. If, as in the series under review, the prækordial electrode is paired with the left lower limb, the tracing will be modified by the potential variations of the limb, and as this is almost always positive during the QRS interval and during the T wave, the result will be a shift towards negative voltage in the cardiogram; and a fictitious absence of the R wave or inversion of the T wave will sometimes occur. The error from this source is equal to one third of the algebraic sum of standard leads II and III. The necessary correction would be relatively simple if it applied to the summits of the waves. Unfortunately it applies only to the height of the wave at a given moment of time and as the summits of the three leads concerned are not in phase and usually do not coincide, the correction is too complicated for routine practice. In all cases in the present series where an abnormality was present or suspected, the above correction was, however, applied before interpretation of the findings. A better method is to pair the prækordial electrode with a neutral area (Wolferth and Livezey, 1944), or, as we now prefer, a central terminal such as Goldberger's modification of the Wilson assembly (Goldberger, 1942).

Brief mention must also be made of the points chosen for the prækordial electrode. In

their supplementary report (1938) the committee of the American Heart Association recommended a number of standard positions related to the surface markings of the chest wall irrespective of the size and position of the heart. Thus the committee recommended that the fourth position be at the intersection of the left mid-clavicular line and the fifth space, and that the third position be midway between this point and the left border of the sternum in the fourth space. As, however, the aim of this investigation was to study the electrical field overlying particular areas of the heart's surface, it was thought desirable that the points selected on the chest wall should bear as constant a relationship as possible to the anatomy of the heart. It has, therefore, been the practice in all the cardiograms now under review to take the fourth chest lead from the outer border of the cardiac apex instead of from the mid-clavicular line whose relation to the heart is variable, and to take the third chest lead from a point midway between the apex and the left sternal border in the fourth space. In cases where the impulse cannot be clearly felt the apex is assumed to be in the mid-clavicular line.

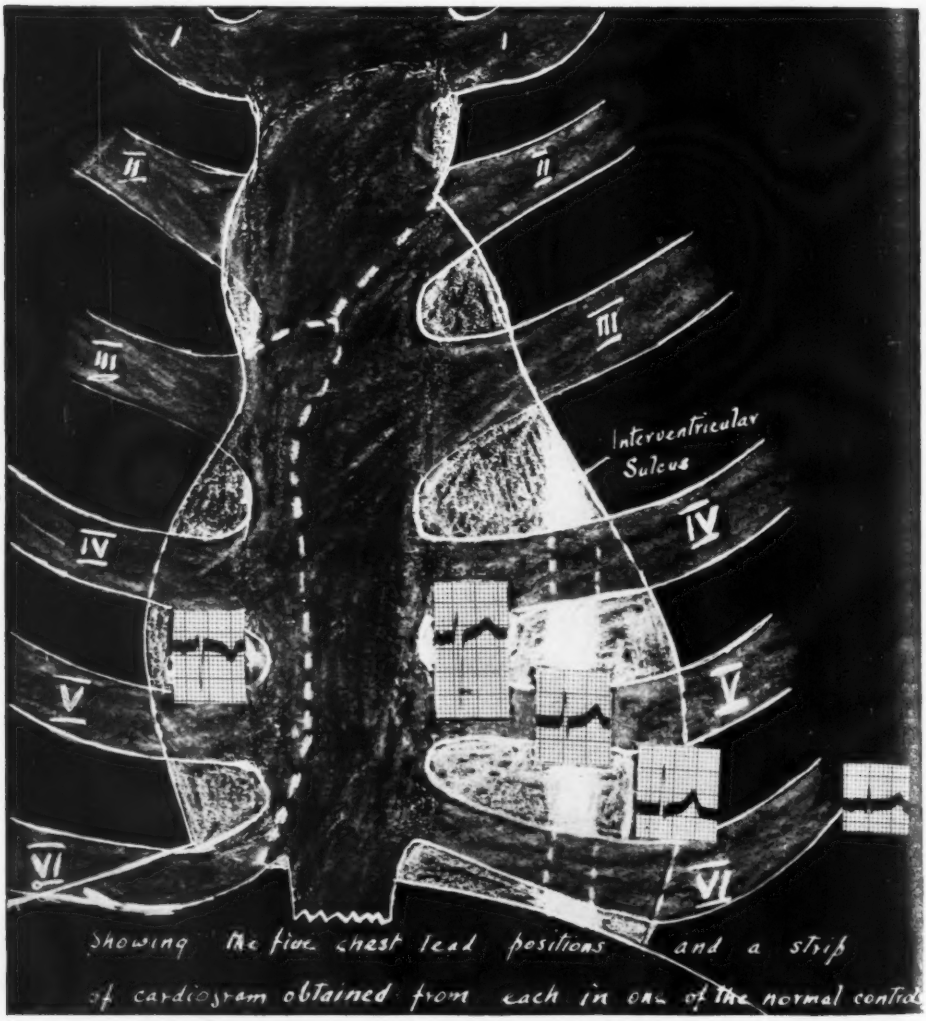


FIG. 1.

This method has also the advantage that the fourth chest lead is identical with lead IV, provided it has been paired with the same indifferent electrode. This is of some importance when a comparison is being made with other cardiograms where only one præcordial lead has been taken. In all other respects the recommendations of the committee of the American Heart Association have been followed. The five points are indicated in the figure by portions of the cardiogram obtained therefrom in a normal subject.

The following is a study of 302 cases in which five chest lead cardiograms CF 1, 2, 3, 4, and 5 were taken and in which full clinical histories were available. They include 218 cases from private practice, being all the cases in which a cardiogram was considered necessary between certain dates, 78 hospital cases, and 6 normal controls. The hospital group comprises all the cases in which a cardiogram was taken during a limited period when all cardiograms were taken with multiple chest leads. With the exception of the 6 controls they all had real or suspected heart disease, but otherwise they were in no way selected. In a short series the average time required for the taking of the five chest leads after the completion of the standard leads was four minutes. All the cardiograms were re-examined and classified under nine headings according to the diagnostic information gleaned from the standard leads on the one hand and the chest leads on the other. In making the classification the standard lead cardiogram was considered doubtful when the QRS complexes were of low voltage (total deflections of the three leads less than 15 mm.), or when the R S–T take off was depressed 1 mm. in leads I or II, or the T wave in these leads measured only 0·5 mm. Ventricular preponderance was considered abnormal, but axis deviation without T wave inversion or significant R S–T displacement was ignored. The chest lead cardiogram was considered doubtful when the maximum T wave was between 1 and 2 mm. or where splintering without widening occurred in one of the S waves from the right side of the heart or where there was a dip of 1 mm. in the R or T gradients.

TABLE I

A Comparison of the Frequency with which Abnormalities were revealed by Standard and Chest Leads in a Series of 302 Cases

Standard Leads	Normal	Normal	Normal	Doubtful	Doubtful	Doubtful	Abnormal	Abnormal	Abnormal
Chest leads	Normal	Abnormal	Doubtful	Abnormal	Doubtful	Normal	Normal	Doubtful	Abnormal
Number of cases	122	40	19	29	8	6	3	2	65
Percentage of cases	*41*	*13·5*	*6·5*	*10*	*3*	*2*	*1*	*1*	*22*

Table I shows that the standard leads were normal in 181 cases and of these the chest leads were abnormal in 40 and doubtful in 19; the standard leads were doubtful in 43 cases and of these the chest leads were abnormal in 29, doubtful in 9 and normal in 6; the standard leads were abnormal in 70 cases and of these the chest leads were normal in only 3 and doubtful in 2. Both were normal in 122 cases and abnormal in 65 cases; of these 65 cases the chest leads were considered to yield extra information in 27. These were cases in which an arrhythmia or prolonged P–R interval or ventricular preponderance was the only abnormality present in the standard leads and where the chest leads revealed QRS splintering or a major fault in the R or T wave gradient, amounting in many cases to evidence of infarction. An analysis of the clinical histories of the 69 cases in which the cardiogram was normal in the standard leads and abnormal or doubtful in the chest leads may be set out as follows.

Certain cardiac pathology

Strong history of myocardial infarction with or without angina of effort	32
Congestive heart failure	3
Hypertension with left ventricular hypertrophy	1
Congenital pulmonary stenosis with septal defect	1
Previous history of failure with complete heart block lasting 5 days	1
Asthma with right ventricular hypertrophy	1
Total with definite cardiac pathology	39 (56 per cent)

Probable cardiac pathology

Angina of effort with no clear history of infarction	8
Recent severe rheumatic fever	1
Sternal or præcordial pain probably due to coronary spasm	8
Increasing effort dyspnoea or palpitation	7
Thyrotoxicosis	1
Paroxysmal tachycardia, poor effort tolerance with tic-tac rhythm	1
Congenital aneurysm of descending aorta pressing upon the heart (ruptured three weeks later)	1
TOTAL with probable cardiac pathology	27 (39 per cent)

Possible cardiac pathology

Sternal or præcordial pain probably not cardiac	3
Asthma (heart not screened)	1
TOTAL with possible cardiac pathology	3 (4 per cent)

There were only five cases in which the cardiogram was normal or doubtful in the chest leads and abnormal in the standard leads. The following is an analysis of these.

Certain cardiac pathology

Strong history of myocardial infarction with angina of effort	3
Aortic incompetence and slight right and left ventricular hypertrophy	1
TOTAL	4

Probable cardiac pathology

P–R interval 0·21 sec. (normal P–R interval chest leads)	1

All the cases of myocardial infarction were of the T III (posterior) type.

The above figures show conclusively that where the standard leads are normal or doubtful and the chest leads are abnormal, the clinical findings (except in cases of posterior infarction) strongly support the chest leads. It was noted that the lead from the apex indicated myocardial damage rather more frequently than any other single lead. At the same time, out of 40 cases in which the chest leads provided the sole cardiographic evidence of disease, that evidence was solely present in leads other than the apical in 21. In all but two of these the diagnosis of myocardial damage was supported by strong or fairly strong clinical evidence.

Measurements of the amplitudes of the R and T waves of all the chest leads were made in 192 consecutive cases and in 40 other selected cases. The selected group comprised all the remaining cases with abnormal chest leads (34) and 6 normal controls, three of the latter being tall and slender and three short and broad. If the amplitudes of the R waves in the five chest leads are plotted graphically in order from the 1st to the 5th chest lead, a curve is obtained that represents the distribution of positive potential across the præcordium during the spread of the excitatory process through the heart: for convenience we shall call it the R gradient. Similarly, if the amplitudes of the T waves are plotted in the same order, a curve will be obtained which may be termed the T gradient. Kossman and Johnston (1935), from a study of 30 normal students, observed that " the average voltage of the R deflection increased progressively in the first four præcordial leads and was nearly as great in the fifth as in the fourth." They also noted that " the average voltage of the T wave was greatest in the 2nd and 3rd præcordial leads and showed a progressive decrease in leads taken further to the left." These observations prompted the following study of the R and T gradients.

In slightly more than half (58 per cent of our series) the form of the R gradient supported Kossman and Johnston's findings. But in a considerable number some portion of the gradient was flat or even presented a dip. An analysis showed that the gradient was flat from the second to the third lead in 23 cases (10 per cent of the series), from the first to the second lead in 16 cases (17 per cent), from the first to the third in 6 cases (3 per cent), from the first to the fourth in 7 cases (3 per cent), and from the second to the fourth in 6 cases (3 per cent). In all cases in which the gradient was flat from the first to the fourth leads the amplitude of the R wave was zero, and of the 6 in which the gradient was flat from the second to the fourth chest leads the amplitude was zero in 3 and 1 mm. in 3 cases. In both these groups there was clinical or cardiographic evidence of myocardial damage (apart from the R waves) in all the cases. In 27 cases (12 per cent), a rising or horizontal R gradient was observed to dip slightly and to rise again as the electrode moved further to the left. In 17 cases (7 per cent)

a similar dip was observed in the T gradient and in 6 of these a dip occurred in both gradients together. It should be emphasized that a dip in the T gradient does not necessarily imply inversion. All the cases presenting a plateau or a dip in the gradient were classified under four heads according to whether on clinical or other evidence it was considered that myocardial damage was certain, probable, possible, or absent.

The results are set out in Table II showing the number of cases in each group and the percentage of the various grades of myocardial damage in each group and for the whole series. It will be observed that myocardial disease was present in 46 per cent, and probably in another 14 per cent, these two groups together comprising 60 per cent of the whole series. In the group with a flat gradient from 1 to 2 there were 63 per cent with definite pathology, and 6 per cent with probable pathology, making a total of 69 per cent with definite or probable pathology. In the group with a flat gradient from 2 to 3 the figures were 57 per cent and 17 per cent, making a total of 74 per cent with definite or probable myocardial pathology. In the group with a flat gradient from 1 to 3 the figures were 67 per cent and 16 per cent, making a total of 83 per cent. In the groups with a flat gradient from the 1st to the 4th, or from the 2nd to the 4th, there was, as previously stated, clear myocardial pathology in all cases.

TABLE II

THE ASSOCIATION BETWEEN MYOCARDIAL DAMAGE AND SOME FEATURES OF THE R AND T GRADIENTS

Leads involved		Flat portion of R gradient					Dip in R gradient		Dip in T gradient		Dip common to both gradients	Whole Series
		1 & 2	2 & 3	1, 2, 3	1, 2, 3, 4	2, 3, 4	Greater than 1 mm.	1 mm. or less	Greater than 1 mm.	1 mm. or less		
No. of cases		16	23	6	7	6	10	17	12	5	6	232
Myocardial Pathology	Certain	10	13	4	7	6	6	10	8	1	3	106
		63%	*57%*	*67%*	*100%*	*100%*	*60%*	*59%*	*67%*	*20%*	*50%*	*46%*
	Probable	1	4	1	—	—	1	3	2	—	—	33
		6%	*17%*	*16%*	—	—	*10%*	*18%*	*17%*	—	—	*14%*
	Certain and probable combined	*69%*	*74%*	*83%*	*100%*	*100%*	*70%*	*76%*	*83%*	*20%*	*50%*	*60%*
	Possible	3	5	1	—	—	3	3	2	1	2	55
	Absent	2	1	—	—	—	—	1	—	3	1	38

There would thus appear to be a real correlation between a plateau upon the R gradient and the presence of myocardial damage specially when the plateau involves the 2nd, 3rd, and 4th chest leads. It was noted, however, that such a plateau was in many cases associated with low R wave voltages which are in themselves of some diagnostic import.

It will also be seen from Table II that the incidence of certain myocardial pathology is somewhat higher than the average for the series in those cases showing a dip in the R gradient, whether greater or less than 1 mm. and in those cases showing a dip of more than 1 mm. in the T gradient. The incidence of probable myocardial pathology in these groups as a whole, however, is not significantly above the average for the whole series. It is also apparent that in cases where the dip in the T wave is 1 mm. or less, or where a dip occurs in both gradients simultaneously, the incidence of certain and probable myocardial pathology taken together is below the average. Furthermore, one of the 6 normal cases presented a small dip in both R and T gradients. It was observed that a majority of the dips in the gradients occurred in the third chest lead, which in this series of cases was taken, as previously mentioned, from the region overlying the septum and interventricular sulcus. In this sulcus lies the coronary artery embedded sometimes in a considerable thickness of fat, which, as Kaufman and Johnston, 1943, have pointed out, is a very poor electrical conductor. Thus, not only does the heart muscle in this situation dip slightly away from the chest wall, but there is also interposed the high resistance of a layer of fat. It would seem that this would be sufficient to

account for a dip in both R and T gradients. It would not, however, explain a dip occurring in the second or fourth lead.

In Table III, therefore, the gradients are grouped according to whether the dip occurs in the third lead alone, or whether the second or fourth chest lead is involved either alone or in addition to the third, and the correlation of the two groups with the presence of myocardial damage is shown. It will be seen that when the third lead alone is involved, the incidence of certain and probable myocardial damage is only slightly higher than the average for the whole series. When the second lead is involved, the incidence of certain myocardial damage is 75 per cent, and when the fourth lead is involved, the incidence of certain myocardial damage is 100 per cent in the case of the R gradient and 86 per cent in the case of the T gradient. In the remaining case showing a dip in the T gradient in the fourth lead myocardial damage was considered clinically probable. It was also observed that when there was an R wave, however small, in the first lead and no R or R^1 in the second lead, myocardial pathology was present in every case. It would appear, therefore, that while a dip in either or both gradients in the third lead alone is of little or no significance, a dip of any degree involving the second or fourth lead is strongly indicative of myocardial damage. In clinical practice all the features of the R and T gradients can readily be appreciated by the eye without any graphical plotting and actual measurements are seldom required.

TABLE III

THE ASSOCIATION BETWEEN MYOCARDIAL DAMAGE AND THE POSITION OF THE DIP IN THE R AND T GRADIENTS

Myocardial Pathology	Dip in R gradient			Dip in T Gradient		Whole series
	In 3rd lead only	Involving 2nd lead	Involving 4th lead	In 3rd lead only	Involving 4th lead	
Certain	10 (47%)	3 (75%)	6 (100%)	3 (30%)	6 (86%)	(46%)
Probable	4 (19%)	—	—	1 (10%)	1 (14%)	(14%)
Possible	6 (29%)	1 (25%)	—	3 (30%)	—	(24%)
Absent	1 (5%)	—	—	3 (30%)	—	(16%)

One further comment should be made on the third chest lead. Two cases of marked QRS splintering in this lead were associated with very doubtful clinical histories of myocardial damage. As the examining electrode in this lead is astride both ventricles it is conceivable that some anatomical asymmetry in the arrangement of the conducting mechanism on the two sides may account for such splintering in rare cases. It may not, therefore, necessarily indicate any pathology and pending further investigation it is suggested that this finding be interpreted with caution.

CONCLUSIONS

The principles underlying the interpretation of chest leads are discussed.

The normal R and T gradients obtained from multiple chest leads are described.

An analysis is made of a series of 302 cases in which multiple chest leads CF 1, 2, 3, 4, and 5 were taken, and from this the observations that follow were made.

The chest leads provided the sole electrocardiographic evidence of myocardial damage in 40 cases (13 per cent) and of these the evidence was solely present in leads other than the apical in 21.

When the fourth lead was involved in a plateau or a dip of the R gradient, myocardial damage was present in every case; and when the second lead was involved in a dip of the R gradient or the fourth lead in a dip of the T gradient damage was present in a high proportion of cases.

A dip of the R or T or both gradients in the third lead is a normal finding.

References

Barker, P. S., MacLeod, A., Alexander, J., and Wilson, F. N. (1929). *Trans. Assoc. Amer. Phys.*, **44,** 125.
Committee of the American Heart Association for the Standardization of Præcordial Leads (1938. *Amer. Heart J.*, **15,** 235.
Evans, C. (1939). *Brit. Heart J.*, **1,** 161.
Goldberger, E. (1942). *Amer. Heart J.*, **23,** 483.
Johnston, F. D., Hill, I. G. W., and Wilson, F. N. (1935). *Ibid., J.*, **10,** 889.
Kossman, C. E., and Johnston, F. D. (1935). *Ibid.*, **10,** 925.
Lewis, T., and Rothschild, M. A. (1915). *Phil. Trans. Roy. Soc. Lond.*, Series B, **206,** 181.
Wilson, F. N., Hill, I. G. W., and Johnston, F. D. (1934). *Amer. Heart J.*, **10,** 163.
Wilson, F. N., Johnston, F. D., and Hill, I. G. W. (1935). *Ibid.*, **10,** 1025.
Wilson, F. N., Johnston, F. D., Rosenbaum, F. F., Erlanger H., Kossman C. E., Hecht H., Cottrim, N., de Oliveire R. M., Scarsi R., and Barker P. S., *Ibid.*, (1944), **27,** 19.
Wolferth, C. C. and Wood, F. C. (1932). *Amer. J. med. Sci.*, **183,** 30.
Wolferth C. C., and Livezey, M. M. (1944). *Amer. Heart J.*, **27,** 764.
Wood, P., and Selzer, A. (1939). *Brit. Heart J.*, **1,** 49.

HEART BLOCK IN A DIABETIC WITH ONLY MILD ARTERIOSCLEROSIS

BY

F. DREYFUSS

From the Medical Division of the Rothschild Hadassah University Hospital, Jerusalem

Received May 1, 1945

Adams-Stokes attacks were observed in an elderly diabetic in whom clinical and anatomical manifestations of arteriosclerosis were minimal. A relation, however, between the underlying cardiac disturbance and the metabolic changes of diabetes was evident. Some rather unusual electrocardiograms were obtained during Adams-Stokes attacks. In view of these uncommon features, and since we have failed to find reports of similar cases, it seemed worth while reporting it in detail.

A dental surgeon, 58 years old, was admitted to hospital with mild collapse and heart failure on December 24, 1942. His mother suffered from hypertension and one brother from diabetes.

He was born in Palestine, and had had malaria in his youth. He had never been seriously ill until 1929, when he became diabetic. Thereafter he was under the regular care of his physician, Dr. Korkidi, to whom we wish to express our gratitude for his kind co-operation and for the material provided by him. His diabetes proved to be rather severe, but was fairly well controlled by almost regular insulin injections during the course of many years. Except for a few pyodermic complications (a furuncle of the lip and a phlegmone of the hand in 1936) he had never been obliged to stop work in his dental practice. His blood sugar fluctuated between 167–386 mg. per 100 c.c.; his urine was mostly sugar-free and contained only occasionally 0.1–1 per cent of sugar. Traces of acetone were detected only very rarely. His weight was always normal.

In 1935 he complained of exceptional weakness; his physician noted a slight muffling of the first mitral sound and a blood pressure of 95/70, whereas his blood pressure had always been normal before and remained so afterwards. Later on, no cardiovascular irregularities were observed; examinations of the blood for urea, Wassermann reaction, etc. gave normal results. His pulse rate was usually about 60. He had never had any anginal pain and hypertension was never noted.

In the middle of 1941, when trying a patent medicine for his diabetes on his own initiative (extract of an Indian mushroom (?) according to his description), and discontinuing his usual dose of insulin, he fainted after a few days and had an attack of convulsions accompanied by unconsciousness. After he had regained consciousness, insulin and stimulants were administered. After a few more attacks he was admitted to the Neurological Department of the hospital (Dr. L. Halpern) in May 1942. A thorough examination, including analyses of the spinal fluid, did not reveal any abnormal findings. The Wassermann reaction in blood and cerebrospinal fluid was negative. His blood sugar at that time was 200 mg. per 100 c.c. sugar. A presumptive diagnosis of idiopathic epilepsy was made and treatment was started with impronal (a barbiturate), epanutin, calcium, and parathyroid. Under this treatment a few more attacks occurred.

During the few weeks prior to his admission to the Medical Division, insulin was decreased from 40 to 30 units a day because of a continuous fall in blood sugar. The evening injection on December 23 was given from an ampoule which contained 60 units per c.c. instead of the usual 20 units; as this difference in content was accidentally overlooked the patient got 45 instead of 15 units. Some time later, when feeling that he was " suffering from insulin shock," he took some sweets and glucose. Shortly afterwards a continuous series of convulsive seizures set in accompanied by complete loss of consciousness and of control of the sphincters. During these attacks a very slow pulse was observed by his house physician. Atropine, camphor, glucose intravenously, and ephedrine were subsequently administered but proved to be of little avail. On the following morning when the attacks finally stopped, his blood sugar was 597 mg. per 100 c.c.

On admission the patient was pale, his extremities were cold, his consciousness was normal, his response somewhat sluggish. He did not complain of any pain or dyspnœa. His pupils reacted to light. The lungs were normal. His heart was in normal limits, the sounds somewhat dull, the pulse urea rate 26–28 a minute, the blood pressure 135/45. The liver was slightly enlarged and tender. Blood urea was 67 mg., later 28–42 mg., cholesterol 272–151 mg., each per 100 c.c. X-ray examination of the heart showed slight diffuse enlargement. Urine analysis revealed only traces of albumin in an occasional specimen. A diagnosis of heart block accompanied by Adams-Stokes seizures was made. Fig. 1 confirmed complete heart block auricular rate 86, ventricular rate 17. The blood

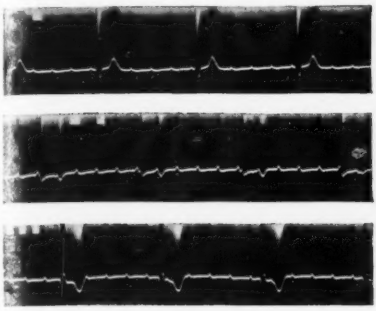


FIG. 1.

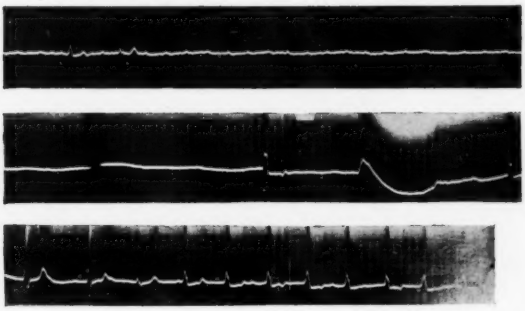


FIG. 2.

sugar was 430 mg. per 100 c.c. at noon. Altogether 40 units of insulin were given. In the afternoon a new series of attacks began: during one and a quarter hours the patient intermittently fell into unconsciousness preceded by a slowing down of the heart action—the critical rate apparently being 22—until the pulse and heart sounds finally disappeared. One cardiac standstill lasted 55 seconds. It is traced in Fig. 2 showing gradual stoppage of ventricular action, and afterwards of auricular action, reaching a complete standstill both mechanically and graphically. After the zero line the film shows one irregular deflection caused by a violent convulsion. Ventricular action sets in, as a result of different pacemakers (Fig. 3), finally at a rather constant rate of 50, whereas for a certain time no sinus pacemaker and no rhythmic action of the auricles can be made out (Fig. 4).

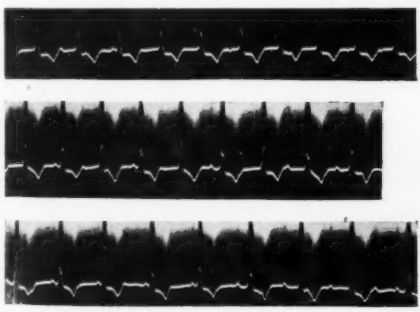


FIG. 3.

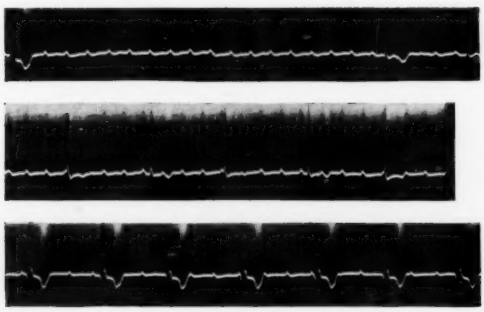


FIG. 4.

Another but shorter attack is recorded showing rhythmic P waves, 92 a minute, and subsequently it changes again to complete block (lead II). Respiration usually faded away a short while before the pulse stopped and breathing recurred increasing in its amplitude before the action of the heart could be noticed again. Thus a perfect Cheyne-Stokes periodicity could be observed, somewhat overlapping the Adams-Stokes periodicity of the heart. Several attacks recurred the following night. After 40 units of insulin the morning blood sugar was 136 mg. per 100 c.c. On the following day no attacks occurred. On December 26 blood sugar in the morning was 370 mg. per 100 c.c.; at noon a series of attacks occurred. It was noted that every time the pulse returned it was quicker, about 36, and sometimes even nearly 50 for a few seconds; furthermore the blood pressure was 150/60 instead of 140/50 before the Adams-Stokes attack. When, subsequently, the diabetes was kept under control,

no further attacks occurred for over a month, although the pulse remained slow. Complete block had become re-established.

Up to January 13, 1943, nothing in particular was noted except a continuous improvement of diabetic tolerance. Insulin was correspondingly decreased to 5–10 units in the morning. On January 13, the patient began to run a temperature of 37·8–38·8 for three days, due to a small pulmonary infiltration. His pulse rate during the course of this complication was 32–38. His diabetic balance was not affected at all and finally insulin was no longer considered necessary (aglycosuria, blood sugar 176 mg. per 100 c.c. on January 28). The patient's diet contained 150 g. carbohydrate, 70 g. fat, 60 g. protein. On February 3, a whole sequence of severe convulsive seizures started without any apparent reason except, possibly, a slight irregularity in his regime. The following morning the blood sugar rose to 500 mg. per 100 c.c., and the patient entered into diabetic coma. 90 units of insulin had to be given, partly intravenously, and the blood sugar was decreased to 310 mg. per 100 c.c. A series of severe attacks led to a state of complete asphyxia and cardiac standstill, lasting about three minutes, and death seemed imminent or had apparently already occurred. An intracardiac injection of caffeine and procardin (coramin) was resorted to and the injecting needle, previously motionless, began to show cardiac contractions, in the beginning at a rate of 60, afterwards decreasing to his usual bradycardia. A short while later, after an injection of insulin, the patient partly recovered consciousness, passing gradually through a state of paraphasia and disorientation to a normal mental condition. As usual, he was completely amnestic as to the entire course of events. On February 8 he had a mild attack, probably as a consequence of an insulin reaction, which was stopped by glucose—an event which occurred several times during this period. A quantity of 25–40 units of insulin applied in three separate injections was necessary to keep the diabetes under a certain, even if unsatisfactory, control—the blood sugar being between 250–300 mg. per 100 c.c., glycosuria between 15–50 g. per day, and sometimes even reaching 80 g. Periods of a few days without attacks alternated with a day or two when attacks occurred. The relation between diabetes and cardiac disturbance became more and more blurred, but it must be stressed, as already pointed out, that satisfactory control of the diabetes was no longer obtained. He was transferred to protamin zinc insulin, 20–30 units. For about a fortnight seizures occurred but rarely; regular insulin 10–15 units had to be added. On March 10 a series of violent attacks began, one rapidly following the other and the patient died on March 13, 1943, without recovering consciousness. Fig. 5, taken during an attack, shows transient ventricular standstill interrupted by isolated ventricular impulses, afterwards ventricular trachycardia followed by decreasing auricular action with complete ventricular

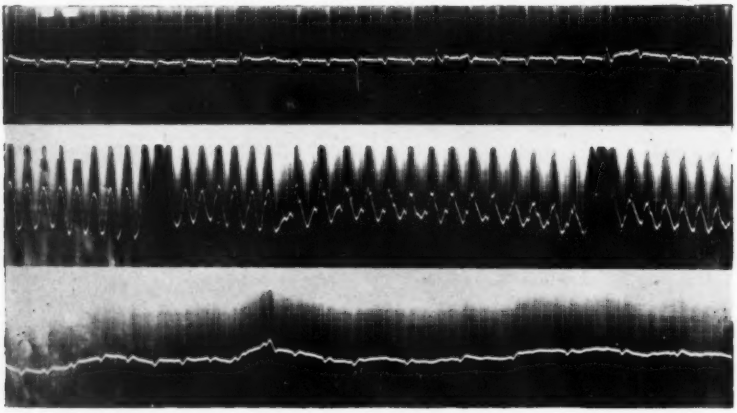


FIG. 5.

standstill. The particular frequency and violence of these attacks may partly be attributed to their occurring during a severe " khamsin " (a hot and dry wind, common in the Eastern Mediterranean), the occurrence of which is often connected with cardiovascular disturbances.

Autopsy (performed by Dr. B. Gellei).

Nervous system: No particular findings.

Cardiovascular system: Heart: slightly enlarged (weight 385 g.) with mild left hypertrophy and dilatation. No gross lesions of the myocardium. Generalized arteriosclerosis of a middle degree

of the aorta with calcified plaques (near to the arteriae iliacae), and of its main branches; mild arteriosclerosis of the coronary arteries.

Lungs: Bronchopneumonic infiltration in the left lower lobe.

Liver and pancreas: No gross findings.

Kidneys: Of normal size, somewhat firm: surface smooth except for scattered areas which are slightly granular.

Microscopic examination.

Heart: Specimens taken from the right and left ventricles, from the A-V node, the A-V bundle and the origin of its two branches, as well as from the lower part of the interventricular septum, showed no pathological changes. Serial sections taken from the A-V system showed no pathological findings. In the right lower portion of the fibrous septum there were several foci of calcification without connection with the right bundle branch. The myocardium is normal. The arteries show very mild arteriosclerosis. Glycogen stain taken from a section of the anterior wall of the left ventricle: glycogen positive, small droplets of glucogen, larger droplets in the part near the myocardium.

Liver: Chronic passive congestion. Plenty of glycogen in the nuclei of parenchyma cells.

Pancreas : No pathological changes.

Kidneys: Apart from mild arteriosclerosis of the large and middle arteries, no changes.

Adrenal glands: Slight hyperplasia of the cortex, at some areas of nodular type.

Lungs: Beginning bronchopneumonia in block taken from the left lower lobe.

Discussion

It is rather significant that the epileptiform seizures, as described by the patient's family, were interpreted as epileptic fits which made their appearance unusually late in life. Cerebral symptoms are not infrequently an initial and outstanding feature in heart disease. Only close observation revealed the true cause of the attacks: the paroxysmal cerebral ischæmia (Fishberg, 1940) being caused by a severe disturbance of cardiac rhythm on the basis of changing degrees of heart block. This block seems to have passed through several stages; it had apparently been of an intermittent nature, in itself a rare occurrence (Comeau, 1937), in a period before, as well as after, the patient's first stay in hospital—his pulse was 60 in the intervals between attacks; A-V block became " complete " and " established ", as Campbell (1944) puts it, at any rate after the patient's second admission to hospital. Typical Adams-Stokes attacks were observed when his ventricles came to a complete standstill, that is to say, when even the ventricular pacemaker stopped its action or its impulse was prevented from spreading over the ventricles (" block in block " (Schmoll)). The sudden onset of ventricular standstill in a pre-existing complete A-V block is an occurrence that requires explanation. The same theories that have been adopted for intermittent interruptions of A-V conduction apply—besides the changes of vagal inhibition—in these cases also. Some subtle local circulatory deficiency as suggested by Carter and McEachern (1934), may prevent the spreading of impulse over the ventricle. Dubbs (1938) rightly sums up the general state of knowledge by confessing our ignorance of the immediate cause of ventricular asystole that leads to the Adams-Stokes syndrome. In one instance at least, even auricular inactivity was demonstrated by a cardiogram that failed to exhibit any impulse (sinus?) whatsoever, thus surpassing in its negativity as an in vivo finding tracings which have been taken even a considerable time after clinical death. In the patient's last days attacks were observed occurring on the basis of ventricular fibrillation which represents another cardiac condition leading to cerebral ischemia.

The explanation for the occurrence of the cardaic disturbance was usually to be found in the fluctuations of diabetic balance. This relation is borne out, for example, by Fig. 6 showing the incidence of attacks and diabetic balance at the beginning of the patient's stay in hospital. The onset of these paroxysms was usually observed when any irregularity in the treatment of his diabetes occurred (overdose of insulin, hyperglycemia). On the other hand, even a short series of attacks tended to derange completely his metabolism to the hyperglycæmic side, thus provoking a rise to more than 500 mg. per 100 c.c. after an attack which had been caused by an overdose of insulin.

It seemed rather natural to assume that arteriosclerosis, especially of the coronary and cerebral vessels, was the underlying anatomical condition of a man, 58 years old, who had

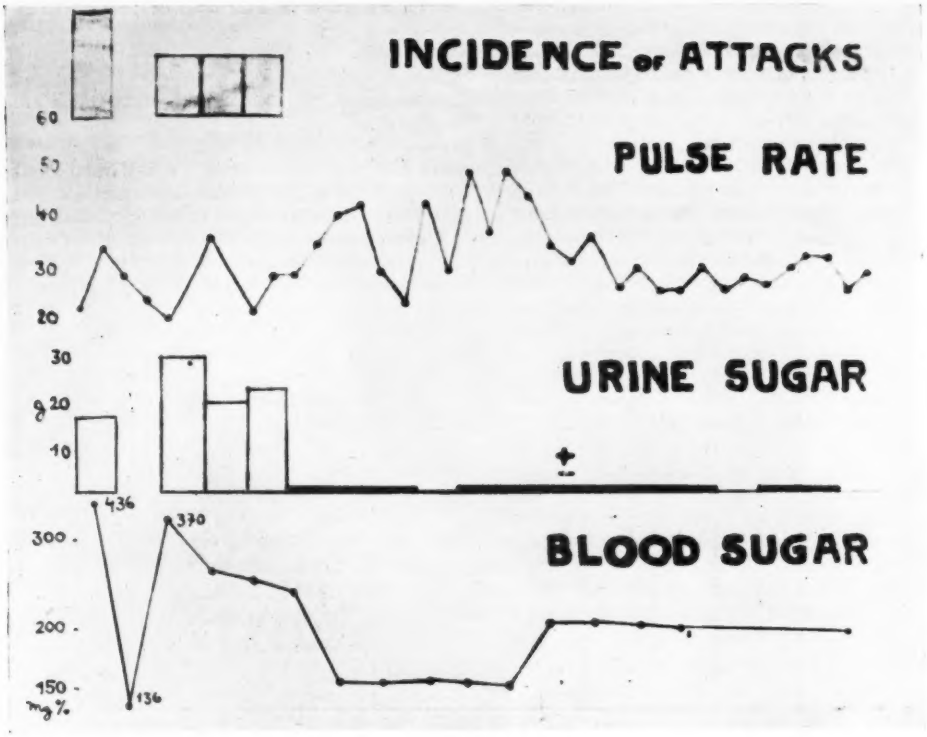


FIG. 6.

been suffering from diabetes for 13 years. Under the circumstances it may be understood that a coronary occlusion was taken into consideration as the possible source of that severe series of attacks provoked by an overdose of insulin the night before his admission to hospital. To our great surprise the findings at autopsy were those of mild arteriosclerosis, in the words of the pathologist, " not even corresponding to the patient's age and by no means explaining the severe disturbances described." In this respect our case bears some resemblance to that of Lawrence and Forbes (1944) suffering from paroxysmal heart block and ventricular standstill, in which post-mortem examination also showed " no gross abnormality of the heart " and the atheromatous changes in the coronary arteries " were not sufficient to obstruct the lumen at any point ". Retrospectively, the absence of the psychic behaviour characteristic of cerebral sclerosis, the absence of retinal signs of this disease, and the lack of anginal pain, should be stressed.

An explanation other than the various changes in the structure and tone of arteriosclerotic vessels must therefore be sought. Taking into consideration the close interrelationship existing between the state of diabetes and the behaviour of the heart, a causal connection between cardiac and metabolic disturbance seems most probable. Under the weight of the overwhelming evidence of arteriosclerosis in diabetics, other mechanisms apt to bring forth such disturbances have been only rarely discussed. A case of transient heart block in a diabetic woman, 56 years old, was reported by Blaisdell (1935). In this case, however, partial A-V block occurred for a short period following coronary thrombosis. Joslin (1940), who lays stress on the " astonishing " frequency of arteriosclerosis as a post-mortem finding in diabetics, mentions also degenerative changes in the myocardium not dependent on coronary disease as having been noted by a number of writers. Nathanson (1932) describes the finding of a pale, swollen, cloudy heart muscle in most cases of diabetic acidosis and coma. In our case,

who only rarely reached the state of intensive acidosis and for short periods only, a metabolic influence upon the cardio-cerebral regulation, according to the clinical observation primarily on the cardiac regulation, may be suggested in the light of the cases described by Shirley Smith (1943). He assumes " that diabetes exerts a deleterious effect on the myocardium, not only by virtue of coronary sclerosis, but also through direct impairment of the parenchyma of the heart ". The maintenance of a sufficient carbohydrate combustion is, in his opinion, at least as important, if not more so, than the provision of an adequate oxygen supply to the myocardium. Deficient carbohydrate utilization is the only feature common to hyper-and hypo-glycæmia and may so, to a certain extent, explain similar cardiographic patterns (especially of the S–T) observed in both conditions and in the same way the observations made in our patient. The nutritional state of the myocardium in this case may be seriously affected by abnormal composition of the blood feeding it, whereupon its irritability and conductivity may be thrown out of order. This may be true particularly of the A-V conduction system, the metabolism of which is probably more sensitive to these alterations on account of the more embryonic nature of its muscle fibres. Harrison and Finks (1943) analogously point out that " fuel deficiency will tend to produce in the tissues metabolic disturbances similar to those induced by oxygen deficiency ". On the other hand, the fact that the patient could be tided over some lighter attacks simply by diverting his attention may point to a cerebral part in this complicated mechanism, the brain in itself being similarly subject to the disturbances of tissue nutrition produced by metabolic fluctuations. This mechanism finally became completely upset, the correlation between diabetes and cardiac disturbance becoming lost; in this last period, however, satisfactory control of diabetes was no longer obtained; cardiac, metabolic, and cerebral regulations became progressively destroyed.

In accordance with these considerations success and failure as to the appearance of attacks were largely determined by the control of diabetes at the corresponding moment. In this respect therapy was successful for a certain time. As a matter of fact, only insulin and glucose respectively were effective in controlling the seizures. Apart from these two substances a good many drugs were given a trial. Since severe arteriosclerosis, as explained above, was assumed to be the underlying condition, doses of several of them were applied rather cautiously; adrenaline and barium chloride were therefore completely excluded. Atropine, ephedrine, erythrol-tetranitrate, and potassium iodide, were of no avail. Aminophylline sometimes seemed to shorten a series of attacks when given into the vein, and definitely influenced only Cheyne-Stokes respiration. Caffeine was successfully used for resuscitation when injected intracardially; it occasionally seemed to shorten an attack. Oxygen did not abolish the attacks but had, at least for a few weeks, a considerable and interesting effect: during its administration no epileptic convulsions appeared and consciousness was usually not lost completely; the pulse did not entirely disappear, but the periodicity of respiration and cardiac disturbance remained uninfluenced. When oxygen administration was stopped, a violent seizure followed almost immediately. This partially modifying action of oxygen has been observed in a similar way by Miller and Fulton (1941). Digitalis had no effect upon the disturbance of rhythm or on the liability to attacks.

A good deal has been written about the relationship of Cheyne-Stokes respiration to Adams-Stokes attacks. Various different patterns of behaviour have been observed and there is no consensus of opinion regarding the frequency of these conditions together: whereas Wenckebach and Winterberg (1927) or Steele and Anthony (1933) remark on the rarity of this coincidence, Price (1927), for example, considers it as a fairly common combination. In the case of Hamburger, Katz, and Rubinfeld (1931–2) " the change in block synchronized with the change in the character of breathing ". A similar occurrence was the one observed in our case.

The case described represents a rare cardio-cerebral complication in a diabetic, the severity of which is illustrated by the violence of the seizures and by the lethal outcome. It belongs to a category of heart disease which, comprising also, among others, heart disease caused by vitamin deficiency, might be designated as " nutritional heart disease "; a classification that points to the nutrition of the heart muscle being at fault—in our case owing to a disturbance of carbohydrate metabolism.

Summary

A case is reported of complete A-V block in an elderly diabetic in whom post-mortem examination revealed only mild arteriosclerotic changes, especially of the coronary circulation. Many series of Adams-Stokes attacks were observed, accompanied by Cheyne-Stokes respiration. These seizures were mostly caused by ventricular standstill and finally also by ventricular fibrillation. These mechanisms are demonstrated by electrocardiograms; in one instance even auricular stoppage was graphically demonstrated.

As the anatomical findings by no means explain the profound disturbances of cardiac action, and as, on the other hand, it was noted that these attacks usually occurred when diabetic balance was seriously upset, an attempt is made to explain the changes in cardiac behaviour by metabolic fluctuations. It is suggested that these fluctuations interfere temporarily with the normal nutrition of the heart muscle, possibly foremost of the A-V conduction system, whenever hypoglycæmia or hyperglycemia prevails.

The applied treatment is briefly discussed.

References

Blaisdell, E. R. (1935). *J. Amer. med. Ass.*, **105,** 1518.
Campbell, M. (1944). *Brit. Heart J.*, **6,** 69.
Carter, E. P., and McEachern, D. (1931). *Bull. John Hopkins Hosp.*, **49,** 337.
Comeau, W. J. (1937). *Amer. J. med. Sc.*, **194,** 43.
Dubbs, A. W. (1938). *Amer. Heart J.*, **16,** 235.
Fishberg, A. M. (1940). *Heart Failure*. London, p. 278.
Harrison, T. R., and Finks, R. M. (1943). *Amer. Heart J.*, **26,** 147.
Hamburger, W. W., Katz, L. N., Rubinfeld, S. H. (1931–32). *Ibid.*, **7,** 498.
Joslin, E. P., Root, H. F., White, P., Marble, A. (1940). *The Treatment of Diabetes Mellitus*, London. Henry Kimpton. p. 437.
Kulbs, F. (1928). *Handbuch der Inneren Medizin*, Berlin. Vol. II, part 1, p. 98.
Lawrence, J. S., and Forbes, G. W. (1944). *Brit. Heart J.*, **6,** 53.
Miller, H., and Fulton, F. J. (1941). *Ann. intern. Med.*, **14,** 2296.
Nathansen, M. H. (1932). *Amer. J. med. Sci.*, **183,** 495.
Price, F. W. (1927). *Diseases of the Heart*. Oxford University Press, p. 208.
Schmoll (quoted from Wenckebach and Winterberg).
Smith, S. and Hickling, R. A. (1933). *Lancet* I, 632.
Smith, K. S. (1943). *Brit. Heart J.*, **5,** 1.
Steele, J. M., and Anthony, A. J. (1933). *Amer. Heart J.*, **8,** 357.
Wenckebach, K. F. and Winterberg, H. (1927). *Die Unregelmässige Herztätigkeit*, Leipzig, p. 389ff.

ARTERIAL THICKENING IN OLD AGE

BY

TREVOR H. HOWELL

From the Royal Hospital, Chelsea

Received May 10, 1945

The pathology of arteriosclerosis has been much studied in recent years: but the clinical aspects have had little attention. A small book on diagnosis written by Parkinson in 1898 had more space devoted to examination of the arteries than Saville's "Clinical Medicine" of 1939, which has six times the number of pages. Even Cowdry's symposium on arteriosclerosis does not say much on the clinical aspects of arterial thickening. In fact, Sydenstricker there quotes the statistics of the Life Extension Institute of America, and gives the final age group as "sixty or over." It is only in this and the following decades that the state of the arteries assumes real importance. It would seem, therefore, that there is a lack of reliable information about the arterial thickening of later life, at least on the clinical side. Apart from a note by Lansbury and Brown about the importance of calcification and the figures of Sydenstricker, there is little in recent papers which bears on this point. The present paper deals with the findings on examination of Chelsea pensioners and offers a new method of classifying arterial thickening in old persons.

STANDARDS

This investigation was one of a series designed to provide data about the normal variations of temperature, pulse rate, blood pressure, arterial thickening, etc., in healthy old persons. Chelsea pensioners, of whom 341 were examined, proved excellent material for this purpose. All were veterans of the old professional British regular army and therefore had been fit, healthy men accustomed to exertion in their early manhood. Before coming to the Royal Hospital, they had to be medically certified as being fit to perform light duties—sick men not being admitted. In addition to being selected material, these men lived a regular life under supervision and medical observation.

Every man in the series under review was given a physical examination, in the course of which his radial, brachial, temporal, and femoral arteries on both side of the body were palpated. The vessels were compressed by the index and ring fingers while the third finger felt the artery and rolled it under the finger-tip. After this, the fingers were rubbed up and down the course of the vessel longitudinally to ascertain the amount of tortuousity or calcification present, as well as the amount of thickening of the wall.

Generally speaking, the brachial arteries showed thickening of their walls more markedly than any others, but calcification was found only in the radial and temporal arteries. Tortuousity was common in the temporal vessels, but also occurred in radials and brachials. In the last two it was associated with at least moderate thickening, which was not the case as regards the temporals. The brachial tortuousity took the form of small segments of a large curve, but the radial curves were often large segments of a small one. Brachial tortuousity was often accompanied by radial calcification. In fact, one group (IV) in the suggested classification was composed of cases showing brachial thickening and tortuousity with slight or patchy calcification of both radials. Examination of the femoral artery gave little additional information as a rule. The fundus oculi was not examined, a previous survey having shown little correlation between the opthalmoscopic picture and the peripheral general arterial state. (Howell, *Brit. Heart J.*, 1942). For classification purposes, the final impression after examining and, if necessary, re-examining the accessible arteries was taken as guide. A few cases were hard to decide, but these mostly had some calcification of one radial with only slight

thickening elsewhere. The classification of arterial changes by age groups is shown in Table I.

TABLE I

ARTERIAL THICKENING IN PATIENTS DIVIDED ACCORDING TO AGE

Age period	Group distribution of each age period in percentages of each age period					
	Total	No. I	No. II	No. III	No. IV	No. V
55–59	3	100	—	—	—	—
60–64	11	27	54	19	—	—
65–69	37	27	19	43	8	3
70–74	146	19	21	48	8	4
75–79	81	8	13	57	15	7
80–84	40	5	10	43	30	12
85–89	20	—	10	40	25	25
90–95	3	—	—	—	—	100
	341					

CLASSIFICATION

Five groups of men were found on analysis of the 341 examined. The first consisted of those without any obvious arterial thickening. The second was composed of those in whom the thickening was slight. The third group, classified as having moderate thickening, had arteries that were easily palpable. The fourth showed thickening of all the arteries examined, with tortuousity in some of them, often accompanied by slight or patchy calcification of the radials. The fifth group had marked calcification present. As may be seen in Table I, there tended to be a steady drift from group I to group V as the age increased. One man, not included in this series, was watched over a period of five years. At the beginning of this time, although his fundus oculi showed arterial changes, there was only minimal thickening of his limb vessels. At the end of the period, he was in group III. Other men observed over a period of three years, passed from group II to group III, from III to IV, from IV to V, and even from III to V during this time. This occurred in ten patients, while ten others remained in the same state as at the beginning of the period. No cases were found to proceed from harder to softer arteries, or from tortuousity to straight vessels, but two doubtful cases were finally settled in group IV, rather than group V.

The first group, those without arterial thickening, was composed of 53 men (Table II), whose ages ranged from fifty-six to eighty-four. Many of the older members did not look their age nor behave in a senile fashion. A few were obese, so that palpation of their vessels was not easy. The vast majority in this group were fit and healthy, only two having physical signs of disease; one had a Plummer-Vinson syndrome, the other had high blood pressure with auricular fibrillation and a large heart.

TABLE II

AGE OF PATIENTS DIVIDED ACCORDING TO GROUP OF ARTERIAL THICKENING

Arterial group	Percentage of each arterial group in each age period				Total	Percentage
	55–65	65–75	75–85	85–95		
I	12	71	17	—	53	15·5
II	10	65	22	3	60	17·8
III	1	54	39	5	159	46·2
IV	—	34	54	12	44	12·9
V	—	24	44	32	25	7·6
					341	100·0

The second group of pensioners comprised 60 men between sixty and eight-five of age. In these cases the arteries could be felt like a thin tape when the vessels were compressed. Any with vessels more prominent than this on palpation were placed in the next group, if more than one artery was affected. The brachials were easier to feel than the radials, while the temporals often had tortuousity, but nevertheless remained soft. The age distribution was similar to that of the preceding class, except that a larger number of men over seventy-five

was met. Only three of the men had a medical history of any significance, two having past cerebral thromboses and one congestive heart failure following hypertension.

The third group was by far the largest. It contained the men with arteries that were thickened, but not tortuous nor calcified. The degree of thickening varied from a sensation as of a soft cord under the skin to that of a tough leathery tube. There were probably several sub-groups not yet clearly defined. The number of cases totalled 159, nearly half the number of men examined. Over 40 per cent of all men between sixty-five and eighty-nine came into this class, but only two were under sixty-five. A great variety of physical states was met in this category of pensioner, varying from perfectly fit healthy old men to those with chronic bronchitis, with old hemiplegia, or with cerebral arteriosclerosis. The younger members of the group were not more clearly healthy nor more conspicuously unfit than their seniors. For this reason it is hard to draw any conclusions about the significance of this degree of arterial change.

The fourth group was composed of 44 pensioners whose ages varied from sixty-six to eighty-nine. More than half the men were over eighty. As the distinguishing feature of the group was the possession of arteries that were thickened and tortuous, with or without slight calcification: it suggests that extreme age, tortuousity, and calcification are connected in some way. The calcification varied from a few hard beads to be felt on rubbing up and down the vessel to irregular hardened areas several millimetres in length. Ten men (23 per cent) in the group were noted as completely fit. The others had signs of past disease or of degeneration such as sclerotic cardiac murmurs, marked effort dyspnœa, hemiplegia, and so on. Some of the pensioners who needed recurrent admissions to the infirmary of the hospital were found here. On the whole, the older men were healthier than the younger ones with this group.

The fifth group included 25 pensioners all of whom showed marked calcification of their radial arteries as well as thickening of their palpable arteries. Their ages ranged from sixty-six to ninety-one, three quarters of them being over seventy-five. All three men over ninety were in this group; but the oldest pensioner in the hospital, aged ninety-six, who was not included in this series, would have been placed in the fourth group. Twelve of the men were relatively healthy and able to get about in comfort. The remainder were more or less infirm, six having only recently returned from the infirmary to which they had been on account of advanced cardio-vascular disease requiring treatment.

Blood Pressure

Each man had a blood pressure reading taken as part of his examination. While a single reading is not satisfactory, it was noted that, in cases where the usual figures for a man were known, there was no deviation from what had been expected. 79 per cent of the pensioners had systolic readings over 160 mm. This was higher than the 50 per cent with similar levels found in 120 successive admissions to the infirmary in 1941–42. The present series, however, deals with the healthy men and not the sick. It was found that in group I, 59 per cent had a systolic pressure over 160 mm.; in group II, 53 per cent; in group III it rose to 80 per cent; in group IV to 84 per cent; and in group V to 96 per cent. The high percentage in the last three groups is noteworthy. About a quarter (24·6 per cent) of the men had their

TABLE III.—Systolic Figures over 200 mm.

Arterial group	Age periods				Total	Percentage of each group with B.P. over 200
	55–65	65–75	75–85	85–95		
I	0	5	1	0	6	11
II ..	0	2	4	1	7	12
III ..	1	24	15	4	44	29
IV ..	0	5	9	2	16	37
V ..	0	3	6	4	13	52
All groups ..	1	39	35	11	86	25
Percentage of each age period with B.P. over 200	7	21	29	50	25	

systolic pressure over 200 mm. In these pensioners, the diastolic figures varied from 100 mm. to 140 mm., only a small number being over 120 mm. Out of a total of 86 patients, 6 were in group I, 7 in group II, 44 in group III, 16 in group IV and 13 in group V. Only 1 was under sixty-five, 39 were between sixty-five and seventy-five, 35 between seventy-five and eighty-five and 11 between eighty-five and ninety-five. These results are shown in Table III.

As may be seen from Tables III and IV, the percentage of men with a systolic figure over 200 mm., rises with age, but later than the percentage of all the men with raised systolic pressure. From these figures it seems that both advancing age and increasingly thickened arteries were associated with a higher blood pressure.

TABLE IV

ARTERIOSCLEROSIS AND RAISED BLOOD PRESSURE (OVER 160)

Arterial group	Age periods				Total	Percentage of each group with B.P. over 160
	55–65	65–75	75—85	85–95		
I ..	1	23	7	0	31	59
II ..	2	19	11	2	34	53
III ..	1	64	54	8	127	80
IV ..	0	13	20	4	37	84
V ..	0	6	10	8	24	96
All groups ..	4	125	102	22	253	77
Percentage of each age group ..	28	68	84	95	77	

DISCUSSION

The first impression arising from the examination of these cases was that the usual procedure of compressing the radial artery at the wrist was not a sufficient guide to the state of the vessels. In some patients there would be neither tortuousity nor calcification in the segment of the artery palpated, and this might give rise to a false estimate of the degree of arterial change present. Examination of both radials and brachials was the minimum which could be of any real value. Also the process of rubbing the fingers up and down the course of the artery gave a lot of information about its condition that was not elicited in any other way. This was especially true when the patient was obese and the vessel not easy to feel. Next, it was found that while there was truth in the general rule that thickening, tortuousity, and calcification grew more frequent with advancing years, yet many exceptions could be met. In fact, there seemed to be a number of men in the eighties whose arteries would not have been abnormal for those twenty years their junior. The group III cases were a real problem. While the proportion of pensioners with raised blood pressure was much higher than in the two preceding groups, and a history of past vascular lesions was not uncommon, yet a number of the men in this group were known to be much more active in body and mind than others of their age. Even among those between sixty and seventy there were about equal numbers of prematurely decrepit veterans and men who were taken for fifteen years less than their true age. The sensation of moderate thickening of an artery covers so many gradations which it is difficult to distinguish that, as stated before, there are probably several sub-groups. As expected, tortuousity and calcification were usual in pensioners over eighty. The ability to express these findings in a simple classification indicates that it has some advantages over the " slight," " moderate," " marked " thickening and " calcified arteries " which are the terms commonly employed at present.

SUMMARY

When the arteries of 341 Chelsea pensioners were examined, it was found that they could be classified into five groups, each with distinct characters; and probably successive stages of sclerotic change. An improved method of clinical examination of arteries is described and its advantages pointed out.

MALIGNANT HYPERTENSION CURED BY UNILATERAL NEPHRECTOMY

BY

C. BRUCE PERRY

From the Department of Medicine, University of Bristol

Received May 30, 1945

The classical work of Goldblatt (1934 and 1937) and of Wilson and Byrom (1939), demonstrating the development of hypertension following unilateral renal ischæmia and the return of the blood pressure to normal following removal of the renal lesion, gave a great stimulus to the clinical study of hypertension. As a result it is clear that in man, as in the experimental animal, renal ischæmia gives rise to hypertension. If the lesion is confined to one kidney and that kidney is removed before permanent hypertensive changes have developed the hypertension may be cured. Many clinical cases have now been investigated and the commonest cause of unilateral renal disease producing hypertension appears to be chronic atrophic pyelo-nephritis (Braasch, 1942). How this leads to renal ischæmia is not clear but Barker and Walters (1940) have suggested that there may be an obstruction to the renal arteries in these cases. Among other conditions found to produce hypertension have been atherosclerosis of the renal artery, pyonephrosis, renal tuberculosis, neoplasm, and trauma. Apparent cure of the hypertension following removal of the damaged kidney was first reported by Butler (1937) in a case of pyelo-nephritis, and similarly successful results have been reported by others. (Patch, Rhea, and Codnere, 1940; Barker and Walters, 1940; Movin, Ohlsen, and Pedersen, 1944; Powers and Murray, 1942; Platt, 1941, etc.)

Successful reports of nephrectomy have also been made in renal tuberculosis (Kennedy, Barker, and Walters, 1941), in tumour (Koons and Ruch, 1941; Richardson and Smart, 1941), following trauma (Farrell and Young, 1942), and in atherosclerosis of the renal artery (Leiper, 1944).

However removal of the offending kidney has by no means always resulted in cure of the hypertension and in some cases in which the immediate effects of the operation were gratifying the blood pressure later returned to the same level as before operation. In 1940 Schroeder and Fish analysed reported cases and laid down the following criteria for operation.

> The onset of hypertension should be recent.
> The renal lesion should be confined to one kidney and should be such that diminution of function has occurred in that kidney.
> Renal function should be within normal limits.
> Retinitis should be absent.
> Arterial pressure should be persistently elevated.

The whole question has recently been reviewed in detail by Sensenbach (1944) who was only able to find 5 cases in which nephrectomy was successful after two years: he agreed in the main with the above criteria. However the cases reported by Platt (1941), by Kennedy, Barker, and Walters (1941), by Powers and Murray (1942) and by Leiper (1944) show that the presence of papillœdema and retinitis (malignant hypertension) is by no means a contra-indication to nephrectomy.

The object of this paper is to report two cases of this type in which the hypertension was apparently cured by unilateral nephrectomy.

Case Notes

Case 1. A man, aged 32, was admitted to hospital on February 2, 1942, with attacks of severe headache and vomiting for about two months. These attacks came on about once a week and his sight gradually became blurred in the left eye. He had had occasional headaches from January till September 1941 when he was discharged from the R.A.F. on account of "low mentality and lack of confidence." In September 1941 he had a sudden severe pain in the left loin, which lasted three days and was so bad that he could not stand. On admission to hospital the blood pressure was 210/130. Both fundi showed papillœdema and small exudates; this was more marked in the left eye which showed a macular star. There was no clinical or radiological evidence of cardiac enlargement. The urine contained a trace of

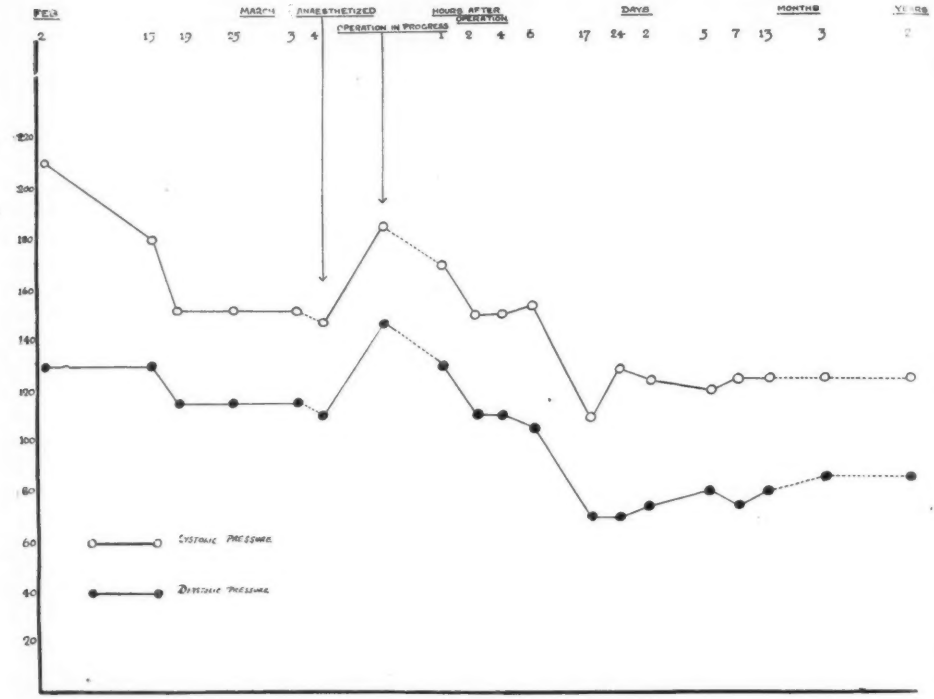


FIG. 1.—Blood pressure readings in Case I.

albumen, but no cells or casts were seen in the centrifuged deposit. Blood non-protein nitrogen was 45 mg. per 100 c.c. The urea concentration in the urine after 15 g. of urea was 2·8 per cent after 1 hour, 2·5 per cent after 2 hours, and 2·4 per cent after 3 hours.

Intravenous pyelography showed very poor excretion of dye on the left side. Cystoscopy showed no abnormality in the bladder, but no dye was excreted from the left ureter 15 minutes after injection, although excreted in 5 minutes from the right side. An ascending pyelogram showed small shrunken calyces on the left side. With rest in bed the blood pressure fell slightly but still remained elevated.

On March 4 a left nephrectomy was performed by Mr. FitzGibbon. The blood pressure fell to normal (115/70) seventeen hours after the operation and was still normal when last seen two years later (125/85). The retinal lesions have steadily improved, the papillœdema and exudates clearing up completely. Vision is still impaired in the left eye.

The pathological report on the kidney is as follows:—"The kidney weighs only 75 grams. This reduction in size is due to the presence of several old infarcts. There is a rim of fresh hæmorrhage just beneath the capsule; presumably due to trauma at the time of operation.

The renal vessels have been divided close to the hilum and the cut ends showed no apparent gross lesion. The pelvis of the kidney gives no sign of dilatation or infection.

Histologically several sections show old healed infarcts but an interesting feature is the presence of large areas of relatively ischæmic kidney tissue, with viable glomeruli lying in a fibrous matrix containing shrunken tubules. One branch of the renal artery, just within the hilum of the kidney, shows a remarkable lesion in its wall. The lumen is patent but narrowed by subintimal fibrosis and between the media and the external elastic lamella is a vascular scar containing some grains of hæmosiderin. This may well represent a healed lesion of polyarteritis nodosa."

Case 2. A Jugoslav merchant seaman, aged 20, was admitted to hospital on February 28, 1944, complaining of severe headache and increasing failure of vision. These symptoms had been present for four months. He had been invalided home from Algiers where he had

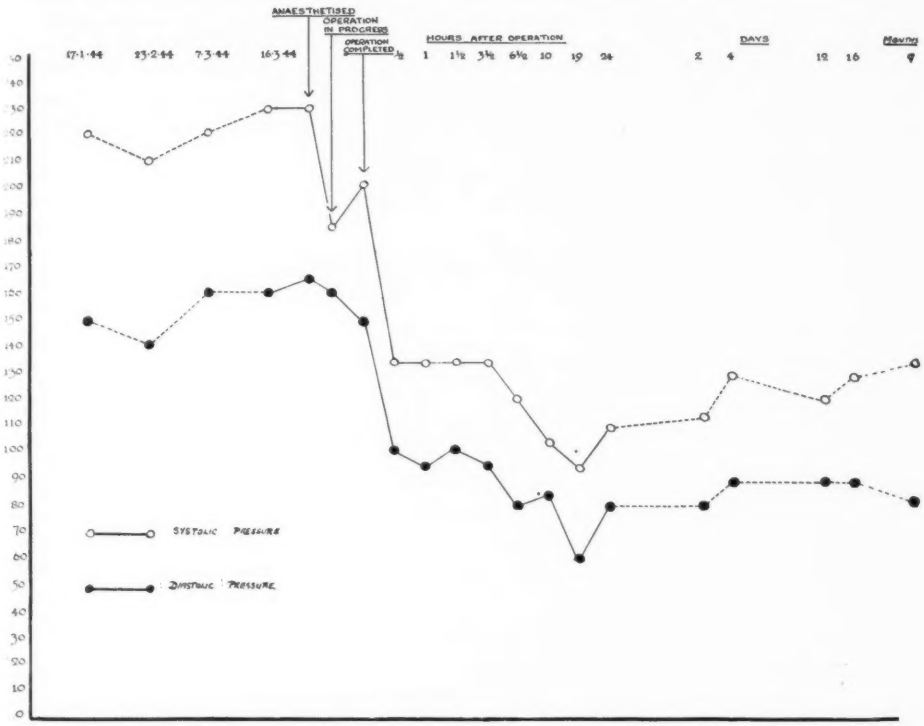


FIG. 2.—Blood pressure readings in Case 2.

been in hospital with infective hepatitis. There his blood pressure was found to be 225/145, the urine contained albumen and a few hyaline casts and the blood urea was 30 mg. per 100 c.c. Five months before he had malaria at Taranto. On admission his blood pressure was 210/140. There was no clinical or radiological evidence of cardiac enlargement. The urine had a specific gravity of 1020, contained a trace of albumen and a few hyaline casts, but was otherwise normal. Blood urea was 40 mg. per 100 c.c. After a litre of water the urine specific gravity fell to 1002 and with restricted water it rose to 1020. There was hypertensive retinopathy more marked in the right than in the left eye. Both discs showed severe papillœdema; the retinæ showed hæmorrhages and white exudates and a macular star. Intravenous pyelogram showed no dye excreted on the left side. Cystoscopy showed a normal bladder with poor flow of turbid urine from the left ureter. No dye was excreted from the left kidney 15 minutes after injection but was excreted in 5 minutes on the right side. An ascending

pyelogram showed a small pelvic shadow on the left side. Rest in bed produced no definite fall in blood pressure.

On March 16 a left nephrectomy was performed by Mr. Cooke. The blood pressure had fallen to 140/100 on return to the ward from the theatre and 19 hours later was 95/60: the next day it rose to 115/80 and on discharge was 130/90. Five days after operation the papilloedema had subsided considerably. It has not been possible to examine this patient again but a report from the Henry Radcliffe Convalescent Home nine months later states that his blood pressure is 135/80.

The pathological report on the kidney is as follows. " The kidney is much reduced in size, weighing only 51 grammes and measuring 8 by 5 by 2·6 cm. The kidney shape is maintained. The capsule strips easily revealing a perfectly smooth surface with no scars or hæmorrhages, but with a small, depressed, yellow infarct at the lower pole; this infarct subtends an area on the surface about 3 mm. square. The vessels are cut off close to the hilum but careful examination deep into the kidney shows no gross lesions in arteries or veins; the arteries have soft thin walls. Histological examination shows that the reduction in size of this kidney is due to a general shrinkage of the epithelium of all the renal tubules. The vessels and the glomeruli are unchanged. The general shrinkage of kidney tissue is what one would expect with partial occlusion of the renal artery; this view of the ætiology gains some support from the presence of an old infarct. The part of the renal artery left attached to the aorta probably bears the cause of the condition."

Summary

Two cases are described, apparently showing complete cure of malignant hypertension following unilateral nephrectomy. In one the renal lesion appeared to be due to infarction but in the other the cause was not determined.

My best thanks are due to the two surgeons, Mr. G. M. FitzGibbon and Mr. R. V. Cooke, who performed the nephrectomies and to Professor T. F. Hewer for the reports on the kidneys.

References

Barker, N. W., and Walters, W. (1940). *J. Amer. med. Ass.*., **115,** 912.
Braasch, W. F. (1942). *Amer. J. Surg.*, **56,** 209.
Butler, A. M. (1937). *J. Clin. Invest.*, **16,** 889.
Farrell, J. I., and Young, R. H. (1942). *J. Amer. med. Ass.*, **118,** 711.
Goldblatt, H., Lynch, J., Hanzal, R. F., and Summerville, W. W. (1934). *J. Exp. Med.*, **59,** 344.
—— (1937). *Ann. intern. Med.*, **11,** 69.
Kennedy, R. L. J., Barker, N. W., and Walters, W. (1941). *Amer. J. Dis. Child.*, **61,** 128.
Koons, K. M., and Ruch, M. K. (1941). *J. Amer. med. Ass.* **115,** 1097.
Leiper, E. J. R. (1944). *Lancet*, **2,** 439.
Movin, R., Ohlsen, A. S., and Pedersen, A. M. (1944). *Acta. med. Scand.*, **119,** 439..
Patch, F. S., Rhea, L. J., and Codnere, J. T. (1940). *Can. med. Ass. J.*, **43,** 419.
Platt, R. (1941). *Proc. Royal Soc. Med.*, **35,** 317.
Powers, J. H., and Murray, M. F. (1942). *J. Amer. med. Ass.*, **118,** 600.
Richardson, G. O., and Smart, G. A. (1941). *Lancet*, **2,** 594.
Schroeder, H. A., and Fish, G. W. (1940). *Amer. J. med. Sci.*, **199,** 601.
Sensenbach, W. (1944). *Arch. intern. Med.*, **73,** 123.
Wilson, C., and Byrom, F. B. (1939). *Lancet*, **1,** 136.

CARDIAC OUTPUT IN A CASE OF PERICARDIAL EFFUSION
WITH A NOTE ON PERICARDIAL PAIN

BY

C. M. FLETCHER

From the Department of Medicine, British Postgraduate Medical School

Received May 28, 1945

The mechanism of cardiac failure in pericardial effusion, which is generally accepted, is derived from the classical experiments of Cohnheim (1889) and Starling (1897) on the effects of injection of oil into the pericardial sac in dogs. They showed that at first the venous pressure rose parallel with the increasing intra-pericardial pressure, the arterial pressure remaining unchanged. When higher intrapericardial pressure was induced, it began to approach the venous pressure, and at this stage a progressive fall in arterial pressure began and continued until the circulation ceased. They explained these observations by supposing that blood was dammed back in the venous system so that cardiac output fell, the arterial pressure being at first maintained by arteriolar constriction, but failing when the fall in output became extreme. No actual measurements of cardiac output were made. The expression "cardiac tamponade" is derived from this conception of obstruction of the venous inflow to the heart.

Kuno (1917) showed that there was a fall of cardiac output with increasing intrapericardial pressure in a heart-lung preparation, but his results are not applicable to the intact animal since he maintained the venous pressure at a constant level throughout his experiments.

Very few observations on circulatory dynamics in pericardial effusion in man have been made. Katz and Gauchatz (1924) made a detailed study of the mechanism of pulsus paradoxus, and showed that the waning of the pulse beat was due to defective filling of the heart during inspiration. Burwell and Strayhorn (1932) and Resnik, Friedman, and Harrison (1935) have measured cardiac output by respiratory techniques in patients with concretio cordis: they showed that it is low, and rises after operative release of the heart. These conclusions are not, however, applicable to cases of pericardial effusion. Recently an opportunity arose of studying cardiac output and right auricular pressures by means of the cardiac catheter (McMichael and Sharpey-Schafer, 1944*a*) with simultaneous measurement of intrapericardial pressure in a case of malignant pericarditis with effusion.

Case History A manageress of a canteen, aged 32, had noticed a painless swelling in the right breast for two years, but had remained in good health till three weeks previously, when she began to become breathless on exertion. During the previous week she had been breathless at rest and her ankles had swollen.

On examination on 24/11/44 she was of normal build. She had severe dyspnœa at rest with orthopnœa. She had a carcinoma of the right breast involving the skin, with secondary enlargement of the right axillary glands and œdema of the right arm. The jugular veins were distended up to 3 cm. above the sternal angle. The cardiac impulse was diffuse, with maximal pulsation in the fifth interspace, 4 inches from the midline. The sounds were normal, but loud and soft beats alternated. There was pulsus paradoxus at the wrist. B.P. 122/88. There were scattered rhonchi in both lung fields with signs of effusion at the right base. The liver was enlarged to 4 cm. below the costal margin. There was slight pitting œdema of both ankles.

An X-ray of the chest showed general cardiac enlargement, with opacity of the right costophrenic angle. An electrocardiogram (Fig. 1) showed electrical alternation with inversion of T in all leads.

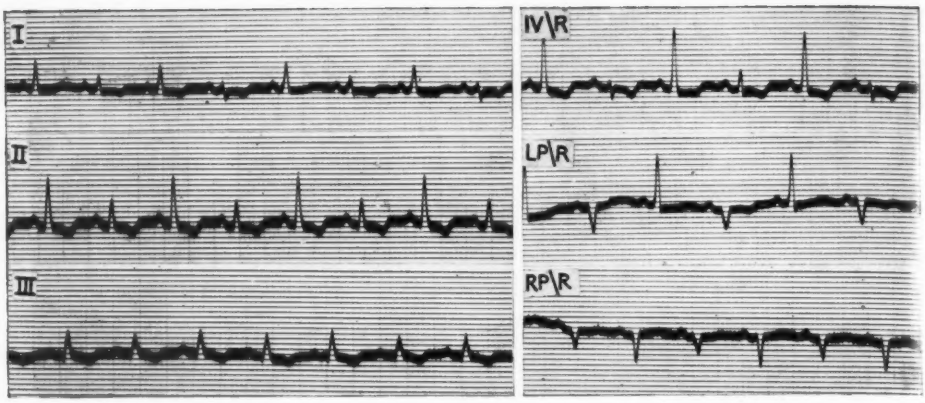


FIG. 1.—Electrocardiogram showing inversion of T in all leads and electrical alternation.

Blood count: Hb. 101 per cent; Red blood cells 5·3 million; white blood cells 11,000.

The diagnosis was malignant pericarditis with effusion.

On 26/11/44 the jugular veins were distended to the angle of the jaw. The patient developed pain in the left chest and a friction rub was heard. Later she had a small hæmoptysis. Digoxin 1·5 mg. was given intravenously. The jugular venous distension fell to a level of 3 cm. above the sternal angle, but there was no clinical improvement.

On 28/11/44, with the patient propped up in bed at an angle of 45° from the horizontal, a cardiac catheter was passed up the left antecubital vein and its tip was located in the right auricle by X-ray. It was connected with a citrate manometer. The right auricular pressure stood at the high value of 15 cm. above the sternal angle. (Normal about 6 cm. below the sternal angle in this position.) There was slight variation in the pressure during the next 30 minutes, but 15 cm. was the average level. The cardiac output was 4·1 litres a minute, which is a low normal figure. A needle was then inserted into the pericardial sac in the fourth left interspace in the mid-clavicular line and was connected to a citrate manometer. The intrapericardial pressure was 7 cm. above the sternal angle. During the next twenty minutes 100 c.c. of heavily blood-stained fluid was allowed to run out of the pericardial sac. At the end of the period the right auricular pressure had fallen to 9 cm. and the intrapericardial pressure to 2 cm. above the sternal angle. Ten minutes later the cardiac output was 3·95 litres a minute (see Fig. 2). During the period of these observations the pulse rate was 124 a minute. The blood pressure was difficult to estimate owing to the œdema of the right arm. The systolic pressure was 122 mm. The diastolic pressure could not be measured satisfactorily but appeared to be 100 mm. After the pericardial aspiration the patient showed a temporary improvement, but then became more dyspnœic, and died five hours later.

In the course of the experiment an incidental observation was made which is of interest. The citrate solution in the manometer was found to be irritant when it escaped into the subcutaneous tissues during the insertion of the catheter (an acid citrate solution, *p*H.4, having been used unwittingly). Each time the manometer was attached to the pericardial needle some of this citrate entered the pericardium and on each occasion the patient complained of pain localized to the outer border of the left upper arm.

Post-mortem, the pericardial sac was distended with 500 c.c. heavily blood-stained fluid. There was a miliary dissemination of secondary deposits throughout the body. There was a large secondary deposit at the root of the pulmonary artery involving the pericardium, which was the source of the hæmorrhagic effusion. The myocardium showed no naked eye evidence of secondary deposits. There was bilateral sero-sanguineous pleural effusion and a large infarct in the left lung.

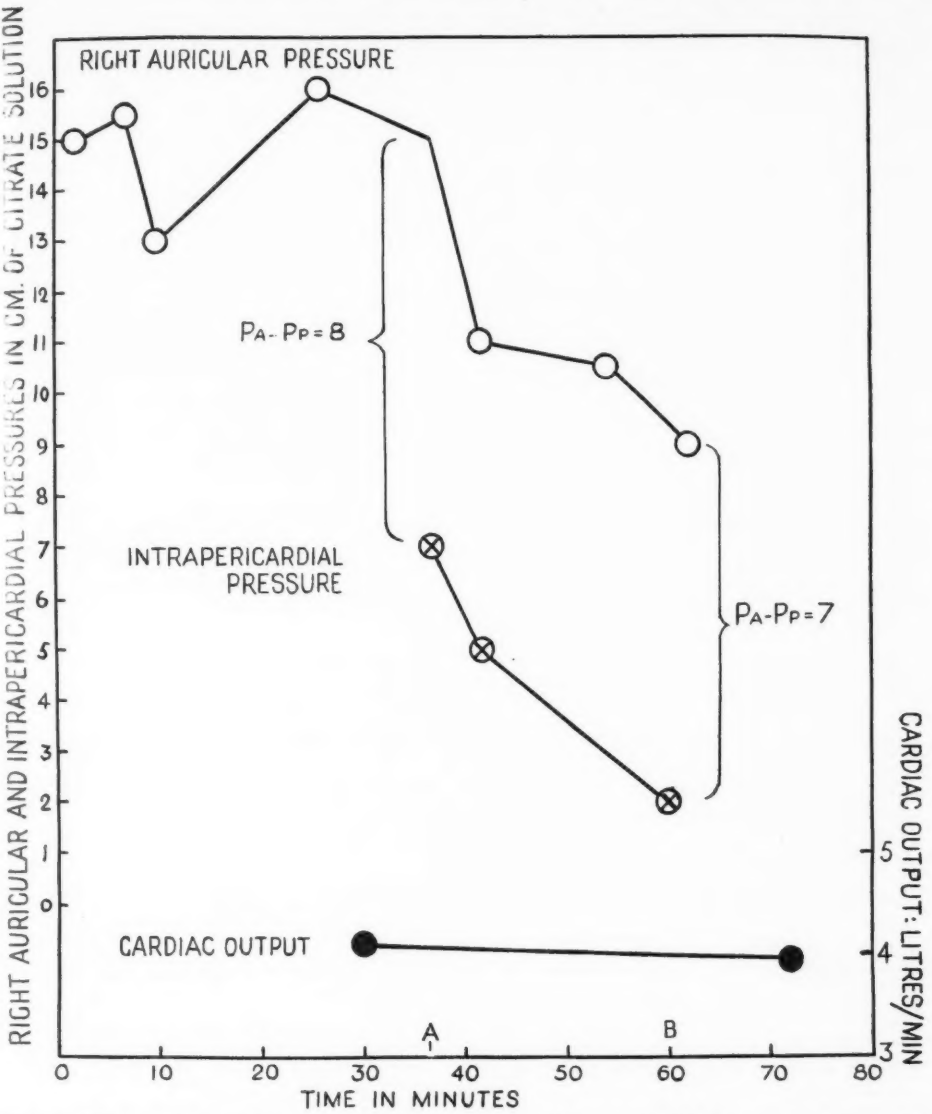

RIGHT AURICULAR PRESSURE
PA-PP=8
INTRAPERICARDIAL PRESSURE
PA-PP=7
CARDIAC OUTPUT
A
B
RIGHT AURICULAR AND INTRAPERICARDIAL PRESSURES IN CM. OF CITRATE SOLUTION
CARDIAC OUTPUT: LITRES/MIN
TIME IN MINUTES
0 10 20 30 40 50 60 70 80
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
3 4 5

FIG. 2.—Effect of pericardial paracentesis on right auricular and intra-pericardial pressures and on cardiac output. The high right auricular pressure falls as the intrapericardial pressure is lowered by paracentesis. Thus the difference between the two pressures (P_a–P_p), which represents the filling pressure of the right auricle is not significantly altered. Cardiac output before and after paracentesis is also unaltered. Between A and B on the base line 100 c.c. of fluid were removed from the pericardial sac.

COMMENT

One of the most important factors that influence cardiac output is the pressure under which the auricle fills. This filling pressure is the difference between the right auricular pressure and the pressure on the outside of the heart. The normal hydrostatic intra-auricular pressure has been measured by Richards, Cournand, Darling, Gillespie, and Baldwin (1941) in six normal subjects and was found to vary between +6·1 and +0·8 cm. of saline with an average of +3·7 cm. The normal mean intrathoracic pressure is also a variable quantity,

but probably averages −6·0 cm. saline (−4·5 mm. Hg., Best and Taylor, 1943). Thus the normal filling pressure of the right auricle has a wide range, but averages +9·7 cm. of saline. In this case of pericardial effusion the filling pressure of the right auricle could be derived from the difference between the right auricular pressure and the intrapericardial pressure ($P_a - P_p$). Before the pericardial fluid was removed it was +8 cm. saline, which is a figure well within normal limits (see Fig. 1). After the fluid was removed the filling pressure was practically unaltered, standing at +7 cm. saline. Associated with this normal and unaltered filling pressure the cardiac output was within normal limits and was also unaltered.

A single observation such as this provides an unsound basis on which to draw any conclusion about the circulatory dynamics in pericardial effusion, but it is interesting to find cardiac output well maintained in a case where the clinical picture was one of cardiac tamponade and to find no alteration in the output when the " tampon " was removed. The output is apparently maintained by the rise of venous pressure, which provides a normal filling pressure for the right auricle. It is clear that any therapeutic measure that may lower the venous pressure, such as venesection or digitalization (McMichael and Sharpey-Schafer, 1944*b*) is contra-indicated. In this case digitalization was certainly of no benefit, although it resulted in no obvious harm. With an increasing effusion, the pericardial pressure will eventually begin to approach the venous pressure, as Cohnheim showed. The output will then fall and the circulation will ultimately come to a standstill. This is presumably what happened terminally in this case, since the pericardial sac was distended with blood-stained fluid post-mortem.

Summary

A case of malignant pericarditis with effusion, presenting the clinical picture of " cardiac tamponade " is described.

Measurements of right auricular and pericardial pressure and cardiac output revealed a right auricular filling pressure and cardiac output within normal limits.

Paracentesis of the pericardium produced a parallel lowering of right auricular and pericardial pressures, so that the right auricular filling pressure remained unaltered. The cardiac output was also unaltered

The suggestion is made that it is only in the agonal stages of cardiac tamponade that the pericardial pressure approaches the venous pressure and that cardiac output begins to fall.

In this case irritation of the pericardium produced pain on the outer border of the left upper arm.

I wish to thank Dr. J. McMichael for his assistance in making these observations.

References

Best, C. H. and Taylor, N. B. (1943). *The Physiological Basis of Medical Practice*. London: Baillière, Tindall & Cox.

Burwell, C. S., and Strayhorn, W. D. (1932). *Arch. Surg.*, **24,** 106.

Cohnheim, J. (1889). *Lectures on General Pathology*, Vol. I. London: New Sydenham Society.

Katz, L. N. and Gauchatz, H. W. (1924). *Arch. intern. Med.*, **33,** 371.

Kuno, Y. (1917). *J. Physiol.*, **51,** 221.

McMichael, J. and Sharpey-Schafer, E. P. (1944*a*). *Brit. Heart J.*, **6,** 33.

—— —— (1944*b*). *Quart. J. Med.*, **37,** 123.

Resnik, L. H., Friedman, B. and Harrison, T. R. (1935). In Harrison, T. R., *Failure of the Circulation*. London: Baillière, Tindall & Cox.

Richards, D. W., Cournand, A., Darling, R. C., Gillespie, W. H. and Baldwin, E. de F. (1942). *Amer. J. Physiol.*, **136,** 115.

Starling, E. H. (1897). *Lancet*, **1,** 652.

TUBERCULOUS PERICARDITIS WITH EFFUSION

BY

PHILIP ELLMAN

From the Leatherhead Emergency Hospital

Received May 28, 1945

This paper deals principally with effusive (rather than constrictive) tuberculous pericarditis, with special reference to a small series of cases that have come under my care since 1941. There is a general belief that tuberculous involvement of the pericardium is very rare, at any rate in clinical practice. In view of the widespread distribution of pulmonary tuberculosis it would appear surprising that the pericardium should be so seldom attacked by the tubercle bacillus and it is of interest to ascertain whether this is, in fact, the case. My impression is that there has been a tendency to neglect tuberculous pericarditis, and to regard it as unduly rare, almost always fatal, and difficult to recognize in the living subject. I hope to show that, in fact, even acute forms of this disease may not necessarily be fatal and that healed tuberculous pericardial effusions may be a not uncommon cause of constrictive pericarditis.

Reported cases and personal communications from morbid anatomists with wide experience of tuberculosis suggest that a diagnosis of rheumatic or idiopathic pericardial effusion (or polyserositis) is made when, in fact, as with a neighbouring pleural effusion, the causative agent is really the tubercle bacillus. Holmes Sellors in his Hunterian lecture (1944) on constrictive pericarditis, not yet published, has emphasized the close relationship of tuberculosis and constrictive pericarditis.

Incidence. It has also been suggested that tuberculosis may follow hard upon rheumatic fever as a cause of pericarditis and that the condition is quite frequently overlooked clinically. Osler (1893) in 1000 autopsies reported 215 cases of tuberculosis in 7 of which (i.e. 0·7 per cent) tuberculous pericarditis was discovered. Norris (1911) in 7219 cases of tuberculosis from Philadelphia hospitals reported 1780 cases of tuberculosis of which 82 (1·1 per cent) had pericardial involvement. Harvey and Whitehill (1937) state that during 45 years 95 cases of tuberculous pericarditis were admitted to the Johns Hopkins Hospital: of these 71 were clinically important, 37 were proved tuberculous, and 34 were unproven, but these resembled in every respect the proven cases; it should, however, be noted that while the death rate of the proven cases was 83 per cent, of the unproven it was only 6 per cent. No other known cause, apart from tuberculosis, was established in the unproven cases. Cultures of the pericardial fluid were sterile but it is, of course, well known that tuberculous pleural effusions are not infrequently sterile on culture. Kornblum, Bellet, and Ostrum (1933) report an incidence in general autopsies of about 1 per cent, while in patients with pulmonary tuberculosis the autopsy incidence of pericardial involvement was 4 per cent. Gloyne informs me that in an analysis of 200 consecutive tuberculous autopsies which he made for Professor Lyle Cummins to compare with primitive tuberculosis in the Rand Native miners only one case was found in this series, as compared with 31 cases in the latter. Suzman (1944) analysed 1893 autopsies at Guy's Hospital and found that of the 102 tuberculous cases 6 (i.e. 6 per cent) had pericardial involvement.

Pathology. As regards the pathology we may recognize three main stages: (1) acute fibrinous (although commonly rheumatic); (2) effusive pericarditis with pericardial thickening; here if the amount of fluid is great there is extensive pressure on the surrounding structures, viz. the lungs, mediastinum, superior and inferior vena cava, mouths of the hepatic veins, together with dangerous pressure on the heart itself and great vessels within the pericardial sac (cardiac

tamponade); large effusions without any appreciable cardiac enlargement are usually tuberculous, and the amounts may vary from 200–3000 c.c.; and (3) constrictive pericarditis (Pick's disease), the effusion having gradually subsided, leaving a greatly thickened pericardium (the effusions become smaller, thick and at times apparently, but not actually, purulent and the go on to fibrocaseous disease). If the condition is survived the adhesive process may progress to a complete obliteration of the sac with the eventual disappearance of the tubercles and caseation, the final result being an apparent non-specific chronic fibrous adhesive pericarditis. It can, therefore, be stated that in the absence of other causes constrictive pericarditis of a so-called non-specific type is probably tuberculous. Holmes Sellors has confirmed a tuberculous ætiology in most of the cases he has studied (i.e. 8 out of 9), and, as he points out, it may be deduced as axiomatic that rheumatic fever, including pericarditis, never produces the constrictive factor.

A primary tuberculous pericarditis may be regarded for all practical purposes as non-existent. Tuberculosis may reach the pericardium (a) by the blood stream, as part of a miliary tuberculosis, or (b) by direct extension from a mediastinal focus. Study of reported cases and autopsy results suggest that the latter is the more likely and generally accepted means of secondary involvement of the pericardium, the infection taking place by extension along the lymphatic channels between the mediastinal glands and the pericardium. This was indisputably so in my own case of tuberculous pericardial effusion and pulmonary tuberculosis which came to autopsy, and in the autopsy report of a case of pericarditis by Barrett and Cole (1944). Direct extension from the lungs or pleura is almost unknown, which would explain the rarity of pericardial involvement without accompanying mediastinal gland involvement.

It seems probable, as Pagel (personal communication) has suggested, that most cases of tuberculous pericarditis occur in the course of an early dissemination following primary infection. The increase in late primary infection corresponds as he suggests with the contemporary rise in the incidence of tuberculous pericarditis in young adults. Cases occurring in the higher age groups and in senile tuberculosis are probably secondary to a tuberculous mediastinal gland involvement with a recrudescence of an early tuberculous process in the glands.

Symptomatology and physical signs of tuberculous pericarditis. These have been admirably described by many observers (Harvey and Whitehill, 1937, Hanneson, 1941, etc.) and I shall confine my attention purely to some points of particular value in clinical diagnosis. Unlike the rheumatic type of the disease the onset tends to be insidious rather than abrupt. There is seldom any considerable degree of local upset: lassitude, asthenia, and a slight evening temperature may be the principal general manifestations. Dyspnœa is not a pronounced characteristic in the cases reported, nor was it in my own cases, unless the effusion is a massive one, and in one such of my own series the patient would not admit to breathlessness and had been at work with this massive effusion right up to the time I saw her. Pain is present in varying degrees of intensity, bulging of the prækordium is noticeable, and there is frequently a cough (due to pressure on the trachea or bronchi), mostly non-productive, but if pulmonary tuberculosis is co-existent there is usually some sputum. In fact, as occurred in one of my own cases, the cardiac complications can be easily overlooked from a clinical standpoint. Often there is no œdema, but when it is present it frequently appears as a terminal event in massive effusions. With the more massive effusions, engorgement of the neck veins, invisible apex beat, diminished expansion, especially of the left hemithorax, together with a bulging of the epigastrium due to liver depression, as I shall describe later in Case 4, may be seen on inspection. Pericardial friction may sometimes be felt at the base of the heart and a palpable apex beat in the normal position may suddenly diminish or disappear as the effusion increases in size. Percussion may reveal a marked increase in the relative cardiac dullness to the right and left—diagnostically this is of the utmost significance. Auscultatory phenomena of distant heart sounds and a friction rub, even on occasions with a large effusion (especially if adhesions are present), may be heard.

An outstanding feature of effusive or even constrictive pericarditis is the complete absence of significant murmurs, particularly noteworthy in view of the apparent size of the heart.

The so-called Ewart's sign, associated with pulmonary compression with bronchial breathing and whispering pectoriloquy at the angle of the left scapula, is sometimes heard. It was present in two of my cases.

A low arterial and pulse pressure and high venous pressure with a quietly acting heart and a paradoxical pulse (radial pulse almost disappearing on deep inspiration) may occur, especially with massive effusions and those going on to the stage of constrictive pericarditis. The so-called Beck's triad in acute and chronic compression is noteworthy. In acute cardiac compression (tamponade) with massive pericardial effusion Beck describes (1) a low arterial pressure, (2) a high venous pressure, and (3) a quiet heart, although Volhard refers more accurately to a small heart. In chronic cardiac compression (constrictive pericarditis) there is (1) ascites and a large liver, (2) high venous pressure, and (3) a quiet heart. This syndrome must not be confused with a polyserositis, i.e. Concato's disease, but it may be consequent upon it (Paul White), as in my own fourth case. Thus, as emphasized by White (1935), Hanneson (1941), and Sellors (1944), polyserositis as a cause rather than effect of constrictive pericarditis is well recognized, but the conditions may merge imperceptibly into each other. With the development of constrictive pericarditis the low arterial pressure becomes associated with a pulse pressure as low perhaps as 20.

X-ray examination of the heart. This is often the only reliable means of early diagnosis and from this point of view we owe much to the comprehensive study of Roesler, to which those interested are referred. With moderate-sized effusions the cardiac silhouette presents a pear-shaped outline in the erect position, the shape changing in the recumbent position to a globular or rectangular appearance. This change in shape with change in position may be of considerable diagnostic significance as will be shown from a description of one of my cases. Fluoroscopy further assists in the diagnosis from gross cardiac enlargement by demonstrating the presence of diminished or even absent cardiac pulsation, both in massive effusive pericarditis and in constrictive pericarditis. Kymography, when available, gives a valuable permanent record of these fluoroscopic findings and Sellors reported it to be of considerable diagnostic value in one of his cases.

Electrocardiographic examination may, as a general rule, be of diagnostic value, often closely resembling that of an acute myocardial infarction with characteristic changes in the R–T segments, in the T waves, and with the low voltage curves in all leads. Unlike myocardial infarction, however, the Q wave is not exaggerated and the direction of the R–T segment and the T waves are the same in all leads.

Diagnostic pericardial puncture. The one infallible diagnostic procedure is the recovery of pericardial fluid by paracentesis, and this can be safely adopted where symptoms, signs, and X-ray examination indicate it. The correct diagnosis is conclusively determined in pericardial as in pleural effusions—and with equal facility—by pericardial puncture. Pericardial paracentesis is always advisable both for diagnostic purposes and to relieve pressure; if excessive some 300–400 c.c. or more may be removed and replaced by half the quantity of air (gas replacement).

The site usually selected is the fifth left interspace outside the apex beat if this is palpable and just over 1 cm. within the outer border of cardiac dullness. Preliminary adequate anæsthestization with 2 per cent novocaine of the skin subcutaneous tissue right up to the pericardium is essential for success, exactly as it is in the case of pleural effusions. Occasionally, where examination shows more fluid to the right or posteriorly at the angle of the left scapula, a site at the fourth right interspace or posteriorly at the angle of the left scapula may be chosen. A 20 or 50 c.c. two- or three-way syringe is valuable if it is proposed to induce a pneumopericardium, and the type of needle used for pleural punctures is adequate as a general rule, unless the fluid is of a thick consistency and the pericardium is thickened, when a wide-bored needle may be essential.

Induction of an artificial pneumopericardium. This measure was first reported by Wenckebach in 1910, and is particularly indicated for large effusions that require repeated tapping on account of rapid re-accumulation of fluid. The fluid is usually replaced by half the quantity of filtered air. Apart from the symptomatic relief my impression that the re-accumulation of fluid is thereby retarded is reinforced by the course of events in one of my own cases. The

chief therapeutic advantages of this procedure may be regarded as the prevention of rapid re-accumulation of the fluid, the prevention of the formation of adhesions by keeping the pericardium distended with air although this is a doubtful sequence, and the demonstration of the size of the heart which is found to be invariably enlarged with a rheumatic lesion and normal or only moderately enlarged with a tuberculous lesion (see Fig. 7B).

Prognosis. The prognosis of pericardial effusions is naturally dependent upon the nature of the effusion, i.e. whether it is clear, hæmorrhagic, or purulent. Most massive clear effusions and some hæmorrhagic ones are tuberculous.

The mortality rate has hitherto been regarded as very high but recent experiences are certainly suggesting modification of this view. In the same way that it is often difficult to recover the tubercle bacillus from clear pleural lymphocytic exudates, which are sterile on culture (now almost universally recognized as tuberculous in young subjects) so with pericardial exudates similar difficulties present themselves. The general impression is that if tubercle bacilli are readily obtained from the pericardial fluid the prognosis is a grave one (Harvey and Whitehill, 1937). In my fatal case the pericardial fluid abounded with tubercle bacilli. Even guinea-pig inoculations are not always successful in isolating the tubercle bacillus, e.g. Suzman (1944) reported a case of tuberculous pericardial effusion, proved at autopsy, where, during life, the fluid was repeatedly sterile on culture, the Mantoux negative, and a guinea-pig test negative on two occasions. Sellors (1944), in a young girl with a massive tuberculous pericardial effusion found on paracentesis that the fluid was negative for tubercle bacilli. Culture and guinea-pig inoculation were likewise negative yet at operation for pericardial resection a few weeks later the pericardium—of the bread and butter type—was found to be riddled with tuberculous lesions.

Barrett and Cole (1944) report a case where the fluid was sterile on culture and where, when it was injected into a guinea-pig the animal maintained health for the unusually long period of five months. Subsequently it died, exhibiting tuberculosis.

In two unproven cases from my own series the fluids injected into guinea-pigs (killed three months after inoculation) were negative but in every way characteristically tuberculous. As far back as 1917, Parkinson (personal communication) reported a case of proved tuberculous pericardial effusion, which I shall quote in greater detail later, where repeated examinations of the pericardial fluid were sterile on culture.

It is therefore obvious that, from the pathological point of view, a negative fluid by no means excludes tuberculosis. On the contrary, where, in spite of a negative fluid, everything else points to the diagnosis of a tuberculous lesion, my impression has been that the prognosis may be regarded as correspondingly more favourable.

Treatment. As with pleural effusions the general constitutional aspect of the case is important. Once the diagnosis has been made in hospital the aim should be a careful sanatorium regime with its strict routine and discipline. From the point of view of local treatment mercurial diuresis may be considered, particularly in polyserositis, while pericardial paracentesis should be repeated where there is a massive effusion. The value of taking the venous pressure and doing an air replacement (pneumopericardium), even if only to determine the size of the heart and the thickness of the pericardium, should be appreciated. Where Beck's triad with chronic cardiac compression originated from a pericardial effusion or a polyserositis (provided that the tuberculous process is reasonably quiescent) surgery, in the form of pericardial resection, should be given serious consideration in view of some of the brilliant results that have been reported (Paul White 1935, Holmes Sellors 1944).

The following case reports will serve as an illustration of some of the points already mentioned.

Case Notes

Case 1.

A factory worker, aged 22, seen in January 1944, gave the following history: three weeks before Christmas she had an attack of " influenza " when she complained of headaches, giddiness, nausea, and tiredness in the legs. These symptoms lasted two days, and a week later she noticed slight swelling of the ankles and dyspnœa. She had no chest pain, palpitation, nor appreciable loss of weight.

A B C

FIG. 1.—Case 1. (A) X-ray of the heart, showing characteristic cardiac silhouette of a pericardial effusion.
(B) The same case following pericardial paracentesis and replacement of fluid by a small quantity of air (pneumopericardium). The comparatively thin pericardial wall is well shown.
(C) The cardiac silhouette is seen, three months later, practically returned to within the limits of the normal.

The past history included measles at the age of four, whooping cough at five, and scarlet fever at seven; there was no history of chorea or rheumatic fever and no family history of tuberculosis. On admission to Leatherhead Emergency Hospital she was obviously ill, pale, and toxic. There was slight cyanosis of the lips, some dyspnœa, and some engorgement of the neck veins, but the girl was able to lie flat. Temperature range 97–100; pulse regular and 120; respirations 24. Mantoux test, 1 in 1000, was positive.

Examination of the heart. Apex beat not palpable; heart greatly enlarged to right and left; area of cardiac dullness 8 cm. to right of sternum and 17 cm. to left; heart sounds faint; rhythm regular; blood pressure 135/100 ; no murmurs heard; no friction audible; signs of compression at the left base.

Fig. 1A shows gross enlargement of the cardiac silhouette, characteristic of a pericardial effusion.

A cardiogram showed low voltage curves and flat T waves in all leads, quite in keeping with pericardial effusion. The T waves were improved in a subsequent cardiogram.

Blood count: red cells 6·5 million; hæmoglobin 56 per cent; colour index 0·4; white blood cells 8500; nothing abnormal in differential count.

Pericardial paracentesis yielded 600 c.c. of clear, straw-coloured fluid which clotted readily on standing: S.G. 1030; total protein 4·7 g. per 100 c.c.; albumin 3·9; globulin 0·8; culture sterile. A pneumopericardium was attempted but she felt faint after 100 c.c. of air had been introduced and it was discontinued (Fig. 1B).

Guinea-pig inoculation: animal killed two months later, no evidence of tuberculosis.

Repeated pericardial paracentesis, performed at intervals, yielded only small quantities of serosanguinous fluid; blood sedimentation rate was 10.

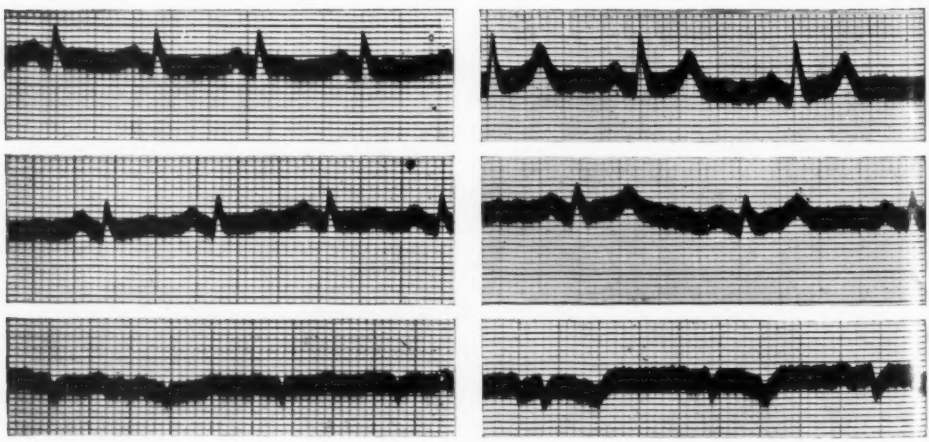
Two weeks later the cardiac dullness had become greatly reduced but pericardial friction now heard to the left of the sternum. In the third month her condition had improved enormously: her pulse rate became normal. An X-ray showed a cardiac silhouette approaching the normal (Fig. 1C). The cardiogram showed better formation of waves T I and T II. On discharge hæmoglobin was 98 per cent.

Seen at regular intervals since her discharge, during which time she has followed a careful sanatorium regime, this girl has no clinical or X-ray evidence of cardiac abnormality and is back at work. I have little doubt that her condition was due to a tuberculous pericardial effusion.

Case 2.

A married woman, aged 34, admitted to the Leatherhead Emergency Hospital complaining of substernal tightness and pain, palpitation, lassitude, loss of weight, and slight breathlessness of three months' duration.

Her previous history was a good one with no evidence of rheumatism. Her mother had died of pulmonary tuberculosis.



A B

FIG. 2.—Case 2. (A) Electrocardiogram before treatment: showing low voltage deflections and slight left axis deviation. (B) After treatment: R is now higher voltage and T I and T II are considerably improved.

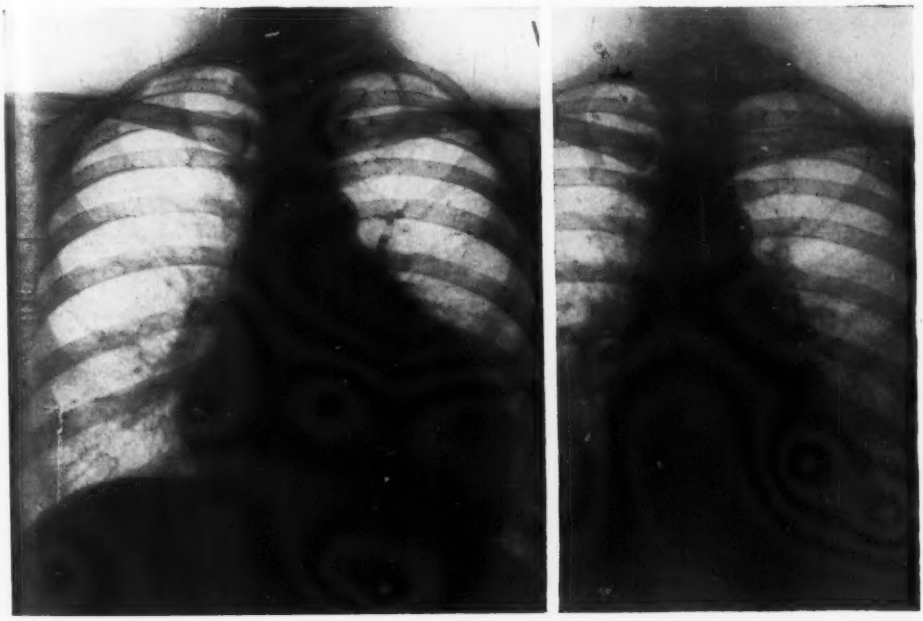
She was not cyanosed; temperature intermittent (97–99·4); pulse 90 and regular; respirations averaged 24; no engorgement of neck veins; blood sedimentation rate 39 ; blood count normal.

Examination of the heart. Apex beat in normal position, but an increased area of cardiac dullness to left and right; no murmurs; pericardial friction heard at base; B.P. 120/90. X-ray examination confirmed the clinical diagnosis of pericardial effusion.

A cardiogram showed small low voltage deflections and flat T waves in lead I. Following treatment subsequent records showed higher voltage curves and improvement in T waves (Fig. 2A and B).

Pericardial paracentesis on two occasions yielded a blood-stained effusion which, on examination, showed a moderate number of leucocytes (82 per cent lymphocytes); total protein 5·8 g. per 100 c.c.; direct smear showed no organisms; culture sterile; guinea-pig inoculation negative after three months.

This case is regarded as a case of tuberculous pericardial effusion in spite of the negative guinea-pig test. Serial clinical, radiological (Fig. 3A and B), and cardiographic examinations have, since her dis-



A B

FIG. 3.—Case 2. (A) Characteristic cardiac silhouette of a pericardial effusion. (B) Showing cardiac silhouette almost within the limits of the normal, following pericardial paracentesis.

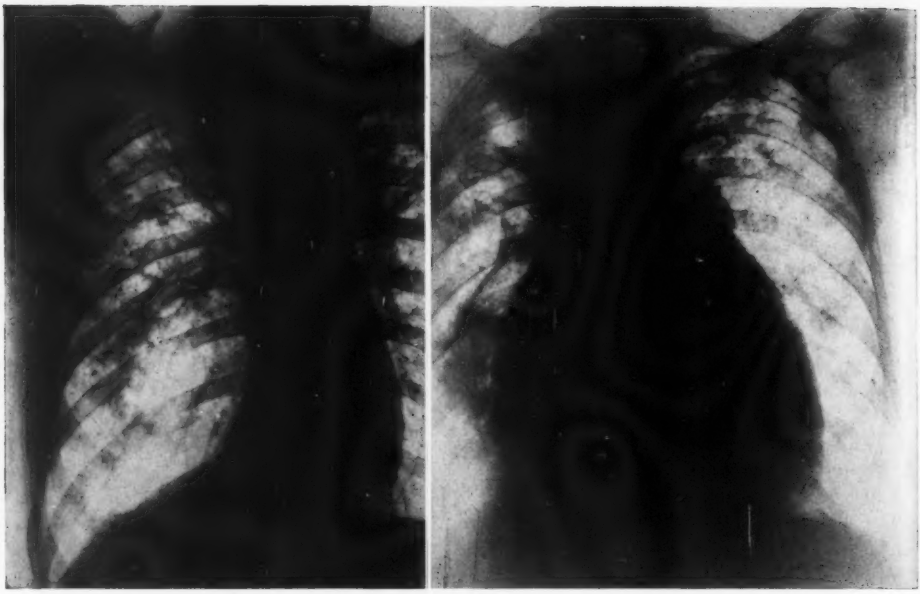
charge nearly three years ago, shown progressive improvement. She now has no symptoms nor any cardiac abnormality.

Case 3.

A labourer, aged 52, had extensive bilateral pulmonary tuberculosis and tubercle bacilli were present in large numbers in the sputum. He was in a sanatorium for six months in 1942, where he made satisfactory progress and gained 1 stone in weight, but the sputum remained bacilliferous. There was then no evidence of any cardiac disease (Fig. 4A).

When seen again a year later he was much worse, was cyanosed, and had a cough with much sputum. Temperature 101; pulse 130; and clinical examination showed obvious re-activation of the disease in both lungs. It was, however, with the greatest astonishment that I discovered on the routine skiagram, in addition to the extensive lung infiltration with cavitation, a cardiac silhouette highly suggestive of a pericardial effusion (Fig. 4B). The patient died in the sanatorium four days later.

Post-mortem examination (confined to the chest). Both pleuræ obliterated by fibrous adhesions; massive caseous glands in both hilar regions. Lungs showed extensive fibrocavernous disease. Pericardial cavity appeared to occupy nearly two-thirds of the thoracic cavity and contained a thick, blood-stained, loculated effusion.



A B

FIG. 4.—Case 3. (A) X-ray of the chest, showing extensive lung infiltration with cavitation, involving upper and middle zones of both lungs. (B) The same case twelve months later, showing extensive lung infiltration with cavitation complicated by a massive pericardial effusion.

FIG. 5.—Case 3. Photograph of the heart and pericardium. The thickened pericardium is well seen, with the characteristic exudate on the surface of the heart and pericardium (bread and butter pericardium).

Dr. J. N. Cummings, who examined the heart and pericardium very completely, also kindly photographed it for me and took sections of the pericardium of which he has been good enough to supply me with microphotographs. He reports as follows on the heart, pericardium, and pericardial fluid.

The heart was considerably enlarged, measuring 14·5 × 10·7 cm. after removal of pericardial sac.

Left ventricle hypertrophied, thickness of left ventricle wall being just under 2·5 cm. from apex. Muscle covered all over by a thick visceral pericardium which varied from 0·5 to 1 cm. and was composed of a granular pink- or grey-coloured granulation tissue. Parietal pericardium grossly thickened, being 0·5 to 1 cm. in thickness and consisting (naked eye) of fibrous tissue and granulation tissue with considerable irregularity of surface. On the irregular surface of the parietal pericardium in the fixed specimen were considerable collections of rather gelatinous material, some up to 1 cm. in thickness (Fig. 5).

Histological examination. Sections were cut of the pericardium, and also of the heart muscle. No tuberculous lesions were found in the heart muscle itself. The section of the pericardium showed a fibrinous exudate lying upon typical tuberculous granulation tissue. Giant cells and tubercle formation could be found with ease. There was a fair amount of mononuclear cellular infiltration throughout. Tubercle bacilli found in some numbers in the section (Fig. 6).

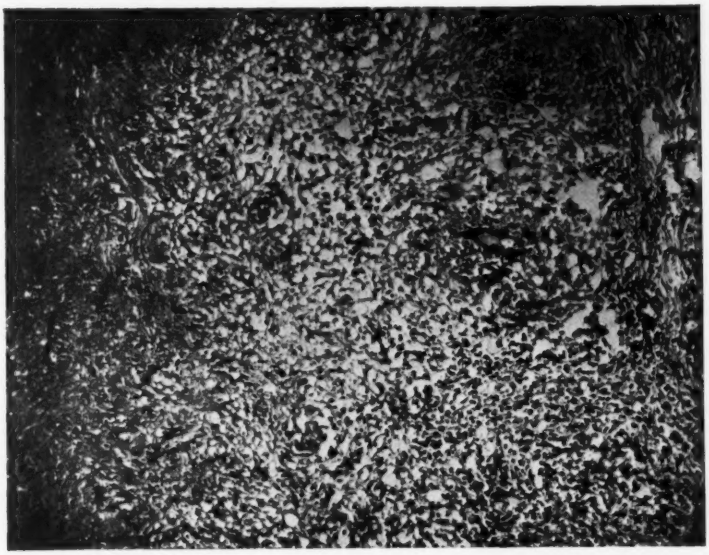


FIG. 6.—Case 3. Microphotograph of the pericardium, showing typical tuberculous granulation tissue and giant cell formation. Magnification × 50.

Pericardial fluid: blood-stained; red blood cells 47,000 per cub. mm.; white cells 900 per cub. mm.; polymorphs 10 per cent; lymphocytes 90 per cent; protein 3·0 per cent; specific gravity 1040; direct smears, a very few tubercle bacilli present; cultures, a fair growth in two weeks.

Case 4.

A gardener, aged 20, had an acute attack of " influenza " in February 1941, after which he complained of increasingly severe breathlessness, a cough with a trace of mucoid sputum, and some swelling of the legs. His previous history showed no noteworthy illness, nor was there anything relevant in the family history.

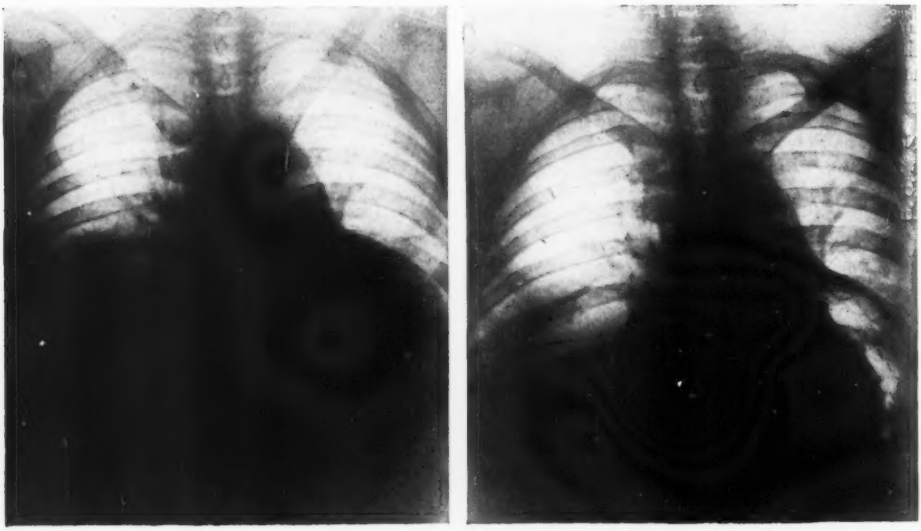
Admitted to hospital seven weeks after onset of illness, very ill and grossly orthopnœic; temperature range 97 to 102·8; pulse 130; no appreciable chest pain; no cyanosis or engorgement of the veins of the neck.

Examination. The chest showed marked limitation of movement on both sides, but especially the left; bulging of the præcordium; marked dullness over the left side up to the second intercostal space; breath sounds absent over areas of dullness.

Heart: apex beat not then palpable; heart sounds distant and feeble; rhythm regular; rate 130; B.P. 130/75; no significant murmurs, but for three weeks after admission pericardial friction heard at base of heart.

Abdomen: ascites; liver palpable; some œdema of legs; urinary output at first diminished bu became normal.

X-ray examination of chest showed a bilateral pleural effusion, particularly marked on left. Afte aspiration of left-sided effusion cardiac silhouette markedly increased and strongly suggestive o pericardial effusion (Fig. 7A).



A B

FIG. 7.—Case 4. (A) The left pleural effusion has been aspirated; the right pleural effusion and the pericardial effusion are well seen. (B) Following pericardial paracentesis and replacement by air: the size of the heart and the thick pericardium are well seen.

Electrocardiogram showed rather low voltage curves in limb leads; T waves in all leads negative, especially præcordial.

All these findings were highly indicative of an acute polyserositis, including a big pericardial effusion, which was confirmed by paracentesis of pleuræ and later of pericardium.

Biochemical and pathological investigations: 21/4/41.

Pleural fluid: clear, straw-coloured, some clotting; polymorphs 2 per cent; lymphocytes 98 per cent; culture sterile; Ziehl-Neelsen, no tubercle bacilli seen; total protein 4·65 mg. per 100 c.c.; serum albumin 2·06; serum globulin 2·59; albumin globulin ratio 0·79.

Pericardial fluid: clear, straw-coloured fluid; polymorphs 90 per cent; lymphocytes 10 per cent; culture sterile; Ziehl-Neelsen, no tubercle bacilli seen; total protein 4·7 mg. per 100 c.c.; serum albumin 1·75; serum globulin 2·95; albumin globulin ratio 0·59.

The differences between the cytology of the pleural and pericardial fluids are noteworthy.

Guinea-pig inoculation with pleural and pericardial fluids both showed tubercle in spleen and lungs.

Urine: albumin, a trace; deposit; an occasional red and white blood cell seen; direct smear, no organisms seen; culture, no growth.

Blood: B.S.R., 34 mm. at end of one hour; hæmoglobin, 78 per cent.

Treatment and progress.

The patient was treated on general lines for his tuberculosis and paracentesis of pleuræ and pericardium were performed. The fluid in the pericardium was replaced by air on several occasions and there was clinical evidence of a hydro-pneumopericardium with characteristic auscultatory physical signs of a " tinkling splash " over the præcordium. He also had a course of salyrgan.

An X-ray film in January 1942 (Fig. 7B) showed a pure pneumopericardium with no fluid and a corresponding disappearance of auscultatory signs. The thickened pericardium was well seen radiologically and the heart did not appear enlarged. Ascites and œdema of the legs had completely subsided. There was a small right pleural effusion, but the left one had resolved completely. He was afebrile and the pulse was 80–100.

His general condition was good: increase of weight; normal blood sedimentation rate and blood count; and repeated examinations of the pleural fluid showed no change in cytology. Examination of pericardial fluid now showed 88 leucocytes per c.mm., now mainly lymphocytic.

The interesting features of the case at this stage were focused on the relatively good, temporary, response to treatment; the original difference in the cytology of the pleural and pericardial effusions; and the question whether the introduction of a pneumopericardium could have any influence in the prevention of chronic adhesive pericarditis (Pick's disease).

The patient spent twelve months in a sanatorium during 1943 and returned to the Leatherhead Hospital in 1944. His progress had been well maintained, but by April he was beginning to develop some engorgement of the neck veins and suggestive evidence of incipient constrictive pericarditis, confirmed by the development of a generalized anasarca with gross œdema of the legs, sacral œdema, ascites, and liver enlargement. He also had a high venous pressure and the circulation time (solution of saccharine, arm to tongue) was 28 seconds.

The possibility of a pericardial resection was under consideration, but in June, owing to the war situation, we were obliged to evacuate civilian patients to the North, where treatment was continued on the lines outlined, pericardial puncture yielding no fluid. He died suddenly in February 1945, and, most unfortunately, permission for post-mortem examination was not obtained. The case appears to have ended in a Pick's disease, secondary to a polyserositis.

Case 5.

A clerk, aged 31, came into Leatherhead Hospital complaining of breathlessness and swelling of the legs and feet. His disability dated back to a cold in 1939, followed by pneumonia, after which

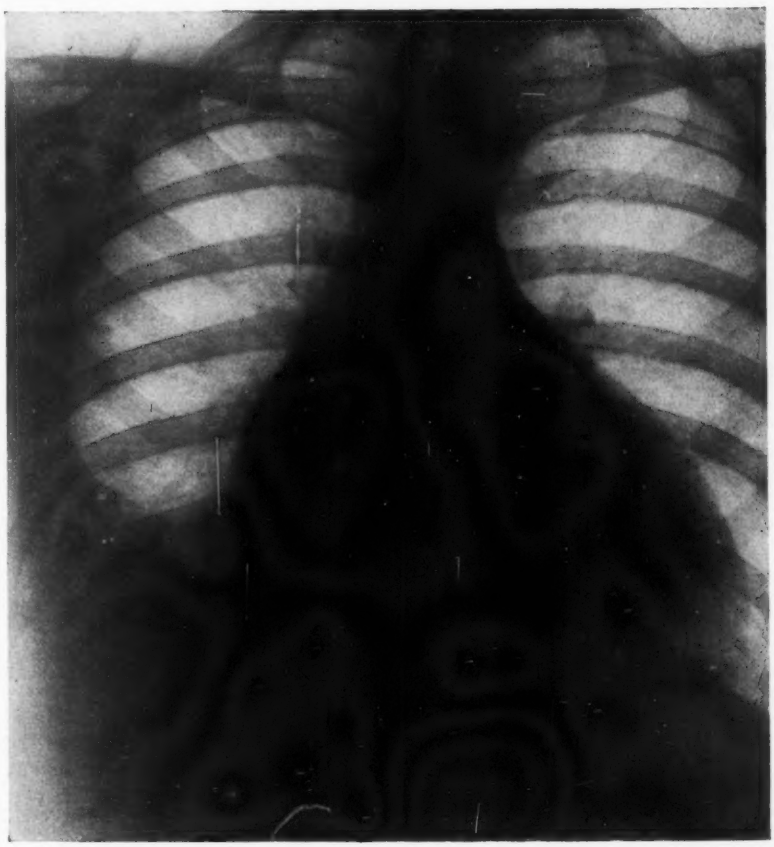


FIG. 8.—Case 5. Characteristic cardiac silhouette of a pericardial effusion with a right pleural effusion: pear-shaped, in the erect position: compare Fig. 9.

he developed a right-sided pleural effusion with the symptoms mentioned. During convalescence the dyspnœa was a constant feature while the œdema was transient. Despite this he had been able to continue with his clerical job. He complained of pain in the form of a " tight constriction " below the ribs on exertion.

On admission he was dyspnœic, even at rest, and had a dry cough causing extreme breathlessness; he was plethoric and generally cyanosed, especially the arms and extremities; no clubbing of the fingers; no history of any acute rheumatism, but a suspicious family history of tuberculosis.

Examination. Neck veins engorged; heart grossly enlarged; apex beat palpable in fifth space, just outside normal limits; increased dullness to right and left; B.P. 120/90; trachea centrally placed; no significant murmurs.

X-ray examination. Cardiac silhouette, gross enlargement to right and left, highly suggestive of a pericardial effusion, pear-shaped in erect position (Fig. 8), but more rectangular in recumbent position (Fig. 9). A noteworthy feature, and of some diagnostic significance, was the marked

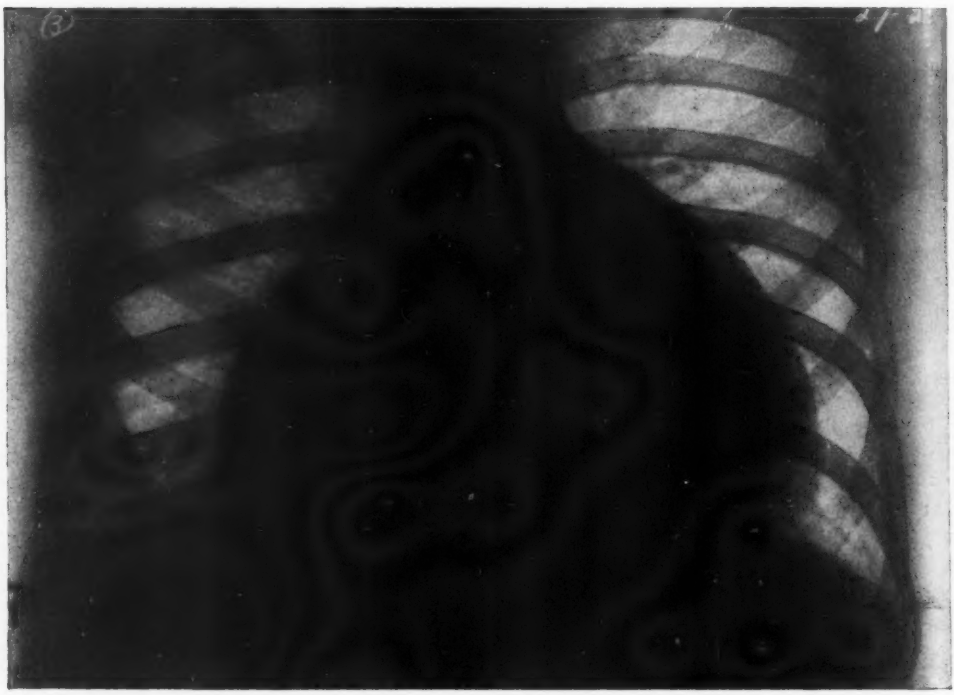


FIG. 9.—Case 5. The same patient recumbent, showing a cardiac silhouette more rectangular in shape.

calcification of the superior tracheo-bronchial glands, specially well seen in the lateral and right anterior oblique positions. Radioscopy showed almost complete absence of pulsation in the lower two-thirds of the right and left borders, but the upper third appeared to pulsate normally.

There was a right-sided pleural effusion which on puncture was straw-coloured, clotted readily on standing, revealed no organisms; sterile on culture; fluid mainly lymphocytic; protein content 4 per cent; blood count showed an erythrocytosis; blood sedimentation rate normal; pericardial puncture yielded no fluid but feel of needle gave impression of an obviously thickened pericardium with, possibly, a loculated or encapsulated effusion. Venous pressure 18 cm. (sodium citrate); circulation time (arm to mouth) 37 seconds (normal 16). Electrocardiogram not pathological.

Liver palpable, 10 cm. below the subcostal margin; gross œdema of legs.

My impression of this case has been that there has been a polyserositis, almost certainly of tuberculous origin—the calcified mediastinal glands seen radiologically give strong confirmatory evidence of this view—and he is now developing a constrictive pericarditis with gross thickening of the pericardium. Fluid may be present, in which case it is either loculated or is so thick that it cannot be aspirated through an ordinary needle. Gross cardiac enlargement (certainly not due to rheumatic

heart disease), complete absence of cardiac murmurs, absence of a rheumatic history, low blood and pulse pressure, absence of cardiac pulsation on radioscopy, high venous pressure and prolonged circulation time, all strongly favour the diagnosis. In view of the problem in diagnosis Dr. Terence East kindly saw this case with me and agreed that, despite the normal cardiogram, the various findings strongly favoured this diagnosis. The patient was to see a thoracic surgeon with a view to a pericardial resection. Unfortunately he is schizophrenic and his confused mental state will not permit this for the present.

Case 6 (*Dr. John Parkinson*).

Whilst discussing the subject of tuberculous pericarditis with Dr. John Parkinson he brought to my notice a case he had under his care during the last war which presents a number of features of such interest that he has very kindly permitted me to quote extracts from it.

The patient, aged 22, was admitted to hospital at Rouen in 1917, ten days after complaining of a "cold", with weakness, cough, and loss of appetite. Previous history was good with no acute rheumatism, chorea, or tonsillitis.

Examination. A fairly well-nourished youth; whole face slightly puffy and glossy, eyelids not more than the rest; cheeks highly coloured, showing, with the lips, a degree of cyanosis. He could lie quite flat in bed but even when supported by two pillows there was slight objective dyspnœa. Only complaints were occasional cough and slight præcordial pain; temperature on admission 100; respirations 34; radial pulse very small, rate being approximately 130 and very irregular.

Examination of the heart showed no præcordial pulsation; area of deep cardiac dullness greatly increased, especially to left where it reached anterior axillary line; second left intercostal space dull to percussion; no abnormal dullness to right. On auscultation: no pericardial rub; heart sounds distant and unaccompanied by murmurs; dullness at base of left lung and in infra-axillary region, with crepitations and diminished breath sounds; bronchial breathing not heard. No abnormal signs discovered in abdomen and no pitting of legs on pressure.

Urine: examined three times, on each occasion a cloud of albumin present on boiling, but no casts found.

Radiographic examination showed pericardial sac greatly distended with fluid and a free left pleura.

Puncture of pericardium: performed five days after admission; 150 c.c. fluid aspirated (clear, except for a few small flakes), the needle showing the movements of the heart as it beat against it. Fluid sterile on culture, despite subsequent positive findings of tuberculosis. Aspiration produced little or no improvement; a course of sodium salicylate likewise unsuccessful.

For two months little change occurred. The patient ate and slept well; temperature irregularly remittent, at time intermittent, reaching 100 to 103 each evening; pulse 120–140 with extra systoles.

The pericardium was punctured on two further occasions; on the first 375 c.c. of clear fluid were removed; on the second 150 c.c. of slightly turbid fluid, but on both occasions it was sterile. During the last two months of his life there was moderate œdema of loins and legs. During the third month of the illness the general condition became worse. The sputum, previously scanty, now became profuse and purulent. When examined a fortnight before death it was found to contain tubercle bacilli. Apart from the signs at the left base nothing abnormal was found on examination of the lungs until the middle of April, when a few rhonchi were heard generally. By this time the patient was mentally dull during the day and mildly delirious at night. He became unconscious and died in May.

Post-mortem examination. This showed, briefly, a pericardial cavity occupying two-thirds of the space of the left pleural cavity and containing 2000 c.c. of dark straw-coloured fluid. The walls of the pericardial cavity were thickened, at some points to the extent of 0·5 cm.; the surface of the heart was covered with thick fibrinous exudate (bread and butter pericardium). The heart was of moderate size with no valvular lesions, and the lung substance showed, fundamentally, miliary tuberculosis.

Summary and Conclusions

Tuberculous pericardial effusions, usually secondary to mediastinal gland tuberculosis, are probably not as uncommon as we have been led to believe. The condition may occur at all ages, and is not necessarily associated with gross symptomatology.

The combination of clinical, radiological, and cardiographic examinations and pathological investigations of the pericardial fluid are of great value in the diagnosis of the disease in the living subject.

Pericardial paracentesis in a suspected case is always advisable for diagnostic purposes and

carries with it no undue risk. A characteristic straw-coloured lymphocytic exudate, as with a pleural effusion, should, despite negative findings for tubercle bacilli and guinea-pig inoculation, arouse very real suspicion of a tuberculous ætiology.

The induction of a pneumopericardium may have some therapeutic value, apart from its diagnostic value in assessing the size of the heart and the degree of thickening of the pericardium.

The relationship of a tuberculous pericardial effusion and polyserositis to a developing constrictive pericarditis (whose ætiology is probably tuberculous) is noted, and the great value of surgery in the quiescent stage of the latter must be appreciated.

The prognosis of tuberculous pericardial effusions, whilst dependent upon the nature of the fluid and the accompanying complications, is not necessarily associated with a high mortality rate. A fluid negative both on culture and to guinea-pig inoculation may occur and yet other diagnostic criteria may point to a tuberculous ætiology. In such cases the prognosis would appear to be correspondingly more favourable.

I am indebted to Dr. Terence East for the electrocardiograms of all my cases; to Dr. David Nabarro and Dr. John Dacie for pathological investigations; to Dr. C. Gray for biochemical investigations and to Dr. J. N. Cummings for photographs of Fig. 5 and 6.

REFERENCES

Barrett, A. M. and Cole, L. (1944). *Brit. Heart J.*, **6**, 4.
Beck, C. S. (1935). *J. Amer. med. Ass.*, **104**, 71.
Gloyne, S. R. (1944). Personal communication.
Hanneson, H. (1941). *Tubercle*, **20**, 79.
Harvey, A. M. and Whitehill, M. R. (1937). *Medicine*, Baltimore, **16**, 45–94.
Kornblum, K., Bellet, S., and Ostrum, T. M. (1933). *Amer. J. Roentgen.*, **29**, 203.
Norris, G. W. (1911). *Cardiac Pathology*, W. B. Saunders & Co., Philadelphia.
Osler, W. (1893). *Amer. J. med. Sci.*, **122**, 6.
Pagel, W. (1944). Personal communication.
Parkinson, J. (1944). Personal communication.
Pick, F. (1896). *Z. klin. Med.*, **29**, 385.
Roesler, H. (1943). *Clinical Roentgenology of the Cardiovascular System.* Thomas Springfield, Illinois, 2nd edition.
Sellors, T. H. (1944). *Hunterian lecture.* Royal College of Surgeons.
Suzman, S. (1943). *Brit. Heart J.*, **5**, 1.
White, Paul (1935). *Lancet*, **2**, 539.